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AN INTRODUCTION

TO

PATHOLOGY AND MORBID ANATOMY.

Ballantyne Press
BALLANTYNE, HANSON AND CO., EDINBURGH
CHANDOS STREET, LONDON

AN

INTRODUCTION

TO

PATHOLOGY AND MORBID ANATOMY.

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THIS SMALL WORK

Is Inscribed

WITH MUCH RESPECT AND GRATITUDE

BY HIS FORMER PUPIL,

THE AUTHOR.

PREFACE.

In the preparation of this, the sixth, Edition of my Text-book of Pathology and Morbid Anatomy, I have been fortunate enough to secure the assistance of my surgical colleague, Mr. Stanley Boyd. The introductory chapter, and the chapters on "Tumours," on "Regeneration," on "Septicæmia and Pyæmia," and on the "Vegetable Parasites," are entirely his work. Most of the new engravings have been drawn from his preparations, Mr. Collings being again the artist.

I trust the work in its revised form adequately represents the present position of the ever-increasing knowledge of the subjects of which it treats; and that it may thus still continue to fulfil the purpose for which it was originally written—that of an Elementary Guide for the Student of Medicine. Should it do so, I feel that it will be largely owing to Mr. Boyd's contributions, and I take this opportunity of gratefully acknowledging his able help.

T. Henry Green.

Wimpole Street,
May, 1884.

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INTRODUCTION.

ANATOMY AND HISTOLOGY investigate the naked-eye and microscopic structure of the healthy body; physiology examines the functions of the parts and elements revealed by them, and studies the chemical processes which constitute healthy life. To obtain a knowledge of disease, parallel courses must be adopted. In post-mortem examinations we note all naked-eye departures from normal anatomy; next, the microscope is employed to show the finer changes to which these departures are due; and, lastly, we endeavour to find out the causes of the abnormal structure and function which constituted the disease, their mode of action, and the nature and sequence of the disturbances which they produce. We thus get pathological anatomy and histology, and pathology—the physiology of disease.

The guiding principle of modern pathology being, that pathology has to deal with no new function or element, but simply with disturbances of normal functions and elements, it is obvious that, for the purpose of studying disease, our acquaintance with the body in health cannot be too intimate.

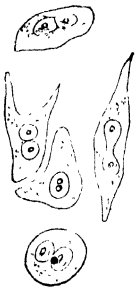
The complex human organism can be reduced to very simple elements — cells and the intercellular substances to which they give origin. These two elements make up every tissue, the cells being sometimes in excess—as in epidermis, where they seem to be in absolute contact—sometimes the intercellular substance, as in the connective-tissues. It is now universally accepted that the cell

is the seat of nutrition and function. Health and disease must be considered as terms referring, not to the body as a whole, but to the cells of which it consists.

Before proceeding to treat of disease we will say a few words upon the constitution of cells in health, and upon their functions and the conditions under which they are physiologically discharged.

CONSTITUTION OF CELLS.—When Schwann established the analogy between the animal and vegetable cell the former was held to be constructed, in all cases, upon the same principle as the latter, and to consist of a **cell-wall** enclosing a cavity in which were contained a **nucleus** and **fluid contents** (Fig. 1). But the fact that no cell-wall can be demonstrated in embryonic cells, blood-corpuscles, and the cells of many rapidly growing new formations, led Leydig and Max Schultze to believe that a little mass of matter, enclosing a nucleus, was all that was necessary to constitute a cell. Max Schultze established the identity of the cell-substance with animal sarcode—a contractile substance existing in the lower animals, and showed that it also was capable of spontaneous movement. He called this substance, of which all cell-bodies, animal or vegetable, are at least at one period of their existence, composed, **protoplasm**; and pointed out that a distinct cell-wall resulted from a retrograde process occurring in its outer layers. Dr. Beale, in this country, promulgated similar views.

FIG. 1.



Cells from a cancer. Showing cell-wall, cell-contents, nuclei, and nucleoli. The nuclei dividing.

The definition of a cell has been still further modified by the discovery that a nucleus is not essential; for none exists in the cryptogamia and in some of the lowest animal forms. In these exceptional cases the cell consists of a simple mass of protoplasm; but in the higher animals the nucleus is almost constant. The cell-wall is

much less so, and must be regarded, in point of vitality, as inferior to the rest of the cell.

Protoplasm is a very complex body of the molecular constitution of which we are ignorant. It contains a large quantity of water, and its solid residue is largely made up of albuminoid material; but with this there are always associated some carbohydrate, fat, and inorganic salts. The relations of these bodies to each other are unknown, but some authorities regard the proteid element as alone essential to the manifestation of life. Protoplasm, as seen in the bodies of normal cells, is generally structureless, soft and viscid, but varying much in fluidity. Granules are frequently present in it, often in one part and not in another, and these probably always differ chemically from true protoplasm. Small cavities, full of fluid, looking like clear spaces, are often seen; they are called **vacuoles**, and may either riddle the cell, or one large one may occupy much of its body. They appear, disappear, and change their position.

In highly specialised cells, protoplasm has acquired a distinct structure—*e.g.*, the fibrillation of muscle and nerve-cells and the striation of many ciliated and gland-cells. In many cells, after hardening in chromic acid, a fine network of fibres is seen in the cell-substance, a fact which has led Klein and others to believe that the protoplasm of cell-bodies is really arranged like a sponge; the interstices being occupied by fluid containing granules which are moved about by contractions of the protoplasm. This view explains many phenomena of cell-life; but, up to the present time, it has not been supported by the observation of living cells.*

Under certain circumstances protoplasm undergoes metamorphoses into various substances—*e.g.*, mucin, globulin, keratin, pepsin and other ferments, glycogen, and fat; which may form large portions of the bodies of cells.

This protoplasm is the essential constituent of the **body** of every cell. In comparison with the nucleus the body varies much in size; being sometimes large in proportion, sometimes quite insignificant.

The **cell-wall**, when present, is of much firmer consistence than the rest of the body, and seems to be due to some metamorphosis of the protoplasm of the latter.

The **nucleus** is more constant than the body, both in size and form. It is usually spherical or oval, but may be quite rod-shaped; is generally placed near the centre of the cell, and may be single or multiple. It resists destructive reagents more strongly than does the body, and in disease often remains after this has been destroyed; it is stained more deeply by carmine and logwood. Its presence may be concealed by fat, pigment, or other substances in the cell-body. The nucleus does not exist in red blood-corpuscles, and it is doubtful whether or no the nucleated red blood-corpuscles of the early embryo disappear or are converted into the non-nucleated discs which succeed them. Those formed endogenously in connective-tissue corpuscles in later fœtal and extra-uterine life are apparently never nucleated. The nucleus of epidermic scales may finally be converted into keratin, and disappear.

The nucleus, which was formerly regarded as a spherical vesicle, bounded by a definite membrane which separated the nuclear fluid from the cell-substance, is now known to possess with great constancy the following much more intricate structure:—1. A membrane bounding it externally; 2, a network of fibres, probably contractile, and certainly capable of great changes in closeness and general form; 3, one or more nucleoli, said by some to be only nodal points in the network; 4, a clear, more or less fluid, substance which fills the membrane and lies in the meshes of the network. The more solid portions—membrane, network, and nucleoli—are spoken of as nucleoplasm; the less solid, as nuclear

matrix. Under Genesis of Cells we shall describe the remarkable changes which occur in nuclei previous to division of cells.

PHYSIOLOGY OF CELLS.—Having described the structure of cells, we will now give a short summary of their normal functions, and of the conditions under which they are physiologically discharged.

A unicellular organism, like the amœba, takes in food, grows, and excretes; performs certain functions, of which motion is the most obvious, and reproduces its like. The whole of this may be regarded as work done, and implies the expenditure of force; and we may be quite sure, although we know nothing of the chemical processes going on in an amœba, that its excreta are simpler compounds than its ingesta—the difference in heat-value between these two sets of compounds representing the force which is available to the organism. The ability to effect these chemical and physical processes, in which the "life" of the animal—as recognisable by us—consists, is inherited, and is spoken of as "**vital activity**," or "**vital energy**." The possession of this is naturally the first essential to living. The other requirements of the cell are a **sufficient supply of suitable food**, and **appropriate surrounding physical conditions**—such as a normal temperature, and suitable density of the surrounding fluid.

In man, a multicellular being, the cells vary much in form and in the results of the chemical actions which they effect. Although retaining more or less independence, varying with the kind of cell, they are bound together for the common good, and each has some special function to perform. Thus there are muscle-cells to produce motion, gland-cells to secrete and excrete, and nerve-cells to control the working of muscle, glands, and perhaps other tissues; certain cells are set apart for reproduction; and, finally, there are the connective-tissues to unite and support the other structures, and surface epithelium to protect them. Thus each kind of work done by the one cell of the amœba is in man performed by a different group of cells

specialised for the purpose. If, then, we recognise the inter-dependences of the cells in the human organism upon each other, and the differences in their structure and purpose in the economy, all that has been said of the amœba will apply to each cell of the body.

The **vital energy** of each cell manifests itself in three channels, spoken of by Virchow as the **Nutritive, Functional,** and **Reproductive Activities.** The two former are purely chemical, and may be considered together. **Food** is taken into the body, digested, and absorbed by lacteals and blood-vessels from the intestines; the various excretory organs give off urea and, in small quantity, other nitrogenous bodies, carbonic acid, and water. Supposing the body to be in **nutritive equilibrium,** neither gaining nor losing weight, the amounts excreted will account for the nitrogen, carbon, and hydrogen taken in as food. Putting aside water, certain salines, and oxygen, which are essential to life, the food-stuffs are albumen, carbohydrates, and fats — the materials of which the body consists. It is evident that a large amount of heat must be set free in the breaking-down of these bodies to the excreta above-mentioned, and this is the source of the force by which every act is performed. The blood carries the prepared food-stuffs to the capillaries, where they pass out with the lymph to come into actual contact with the cells. Certain, or all, of these bodies are now taken up, and become *part of the substance* of the cell, replacing some older material which has been broken down to supply force for assimilation and all other actions of the cell. This breaking-down of cell-substance consists in the union of it with oxygen obtained from the blood, and stored by the tissues in some unknown way. All such oxidation processes are believed to take place *in* the cells, *not* in the blood; and this almost necessitates that all food shall become part of a cell before it is oxidised; it is not oxidised directly. Although the food-stuffs and the tissues of the body are composed of the same chemical

compounds, it is certain that waste of any one of these is not repaired by a process of simple replacement by a like compound from the food. Fat, *e.g.*, taken into the body is certainly not laid down as fat in the connective-tissue. It is probable that many changes in the arrangement of the elements of food-stuffs occur before they form tissue both analytical and synthetical, and force is thus alternately liberated and rendered potential; but this does not affect the main fact that the body ultimately obtains the force equivalent to the difference in heat-value between the ingesta and excreta.

We have enumerated the compounds presented to cells in lymph, and also those which leave the body as the ultimate products of cell-action, but in no instance do we know the connecting links between the end-products. Whilst the ingesta of cells must be tolerably uniform in character, their excreta are probably as various as are the uses of the cells in the body—witness the different compositions of the many secretions, and the unequal distribution of the extractives, such as kreatin, xanthin, &c. The breaking-down of tissue or **waste**, which is going on constantly on the one hand, and the building-up or **repair** which in health keeps pace with it, on the other, constitute the **nutritive exchange** of the cell or of the whole body. This process is constantly being disturbed from pathological causes; whilst, physiologically, formation exceeds waste during the period of growth, but the opposite obtains in old age, when the vital energy of all cells is failing, and their functions are imperfectly discharged.

In order that the nutritive exchange of the cells of the body may be normal, the same conditions must be present which were stated to be necessary for the healthy life of an amœba. These conditions were—the possession of normal vital activity or ability to effect chemical change; a sufficient supply of food of suitable quality, depending in man upon the circulation and blood constitution; and the presence of appropriate surrounding physical conditions. To these must be added—in the case, at least, of nerves,

muscle and certain gland-cells—connection with a healthy nervous centre. When motor nerve-fibres are cut off from the ganglion-cells of the anterior cornu, or when sensory are severed from those of the posterior spinal ganglion, they rapidly atrophy, the axis-cylinders being probably long processes of these cells. Section of a motor nerve causes atrophy of the muscles supplied by it, and section of the chorda tympani is followed by wasting of the submaxillary gland. Each of these tissues has an active function to perform, but physiologically this function is never performed except in response to nervous stimulus. Removal of this consequently checks or annuls their nutritive exchange, and deprives them of the afflux of blood which accompanies their action. In the above instances, the nervous system undoubtedly exercises a **trophic influence,** though not by means of any special trophic nerves. It is said by some to have the same influence over all the cells of the body; but this is denied by others who fully allow its power over nerves, muscle, and such glands as secrete physiologically only in response to stimulation of special secretory nerves. The question at issue is—*whether the nervous system influences those chemical changes in which the life of cells, other than gland, muscle, and nerve, consists.* The discussion is carried on mainly with reference to the "non-working cells"—connective-tissue and epidermic. Can the nervous system increase the vital energy of a cell, and cause it to assimilate more food, to grow and multiply? Can it inhibit the performance of these functions and produce atrophy? Or, can it so change the metabolism of cells that their products become irritating and cause inflammation? The question is a very important one, and cannot at present be decided; but the arguments on each side will be given.

In the first place, a general objection has been raised to experiments having for their object to prove the presence of special trophic nerves—viz., that the influence of other kinds of nerves, especially vaso-motor, has not been eliminated. It is necessary to remember always that after sec-

tion of the nerves of a limb the part beyond is insensitive, its muscles never contract, the afflux of blood which accompanies their action is lost to the part, and the venous circulation no longer receives help from them. Its vessels at first dilate when the central control is removed, and the part reddens and warms from flow of a larger quantity of blood through it; but soon the general increase of tonus compensatory to the local diminution dies away, the vessels of the part remain dilated, and the flow through them becomes slower than natural; consequently the part is cold, and pale or bluish. After a time, however, the local vascular nerves gain power, and a certain amount of tonus, which is easily upset, is restored. As a result of these changes in the nutritive and physical conditions of a part, many changes in it are easily explicable without calling into existence a special set of nerves.

The facts which are held to prove the influence of the nervous system on the nutrition of cells in the non-working tissues are the following:—The **fall in the carbonic acid discharge** which occurs when the body is exposed to a high external temperature, and **the increase** which results under opposite conditions, show that diminished and increased chemical changes share with vaso-motor changes the duty of maintaining an average temperature. It seems most probable that the alterations in metabolic activity are owing to nerve-influence; but there is as yet no reason to suppose that this is exercised on tissue other than muscle. It has been above stated that the chemical decomposition which gives rise to muscular contraction occurs physiologically only in response to nervous stimuli, and part of the force liberated appears as heat. It is possible that this decomposition may be effected slowly under nerve-influence without causing contraction, force being manifested as heat only. Perhaps this may be one way in which the rise of temperature in fever is caused.

The **diabetes** which results from head-injuries and from puncture of the floor of the fourth ventricle, seems cer-

tainly to be due to a too-rapid conversion of glycogen into sugar in the liver-cells; and Foster inclines to the view that this is due to the direct action of nerves on the cells. But others connect the abnormal metabolism with dilatation of the hepatic arteries which always results from puncture.

Many **inflammations** of skin, mucous membranes, viscera, bones, and joints, are described as due to section or irritation of trophic nerves.

In some cases of hemiplegia (especially from hæmorrhage), and occasionally from sabre-wounds of the brain, extremely **acute bedsores** form on the opposite buttock; and similar lesions appear over the sacrum in paraplegia from sudden, extensive injuries of the cord. They are distinguished from ordinary bedsores by the early date (second or third day) and acuteness of their onset, and the uselessness of the usual precautionary measures. Cohnheim objects to these, that they are but differences of degree; and that there is no constancy in their occurrence with apparently similar lesions of any particular part of the cerebro-spinal axis. It certainly is strange that trophic influence should be so marked just at pressure-spots. In this class of cases, too, **cystitis and pyelitis** may appear at about the same time as the bedsores, and Charcot thinks that these inflammations are due to irritation of trophic nerves; but, as exceedingly foul urine, which invariably contains organisms, is noted before, or with, the onset of cystitis, others believe that the latter is due to organisms introduced from without (often by a septic catheter), which render the urine extremely irritant by putrefaction. Similar cases occasionally occur after the passage of a few catheters in cases of enlarged prostate.

Trigeminal keratitis, &c.—Intra-cranial section of the fifth nerve causes cloudiness of the cornea in twenty-four hours, and often destructive panophthalmitis; at the same time ulcers appear on insensitive parts of the mucous membranes of mouth and nose. The ulcers in the mouth are probably due to unheeded injuries from the teeth, &c.;

and it is stated that the keratitis can be prevented by most carefully protecting the eye from injury with the still sensitive ear. **Ulcers on the foot,** often progressive, after section of the sciatic are similarly accounted for.

Pneumonia after Section of the Vagi is apparently due to entry of food, &c., through the insensitive glottis, and not to any trophic influence. It has been suggested, however, that the **acute fatty degeneration of the heart,** which is found in these cases, is really due to the removal of some action of the vagi on its tissue.

Erythema, Urticaria, Pemphigus, and especially **Herpes,** may appear in the distribution of nerves, which are the seats of some irritant lesion, as after fractured spine, in locomotor ataxy and other scleroses of the cord, inflammation of the Gasserian or a posterior spinal ganglion.

Serous Synovitis, and Arthritis with rapid painless and great erosion of the articular ends of the bones, may occur in cases of hemiplegia and ataxia, and are supposed to be due to involvement of the cells of the anterior cornu by progressive sclerosis. In both these latter groups of cases a causal relationship between the nervous disease and the peripheral lesion is very doubtful.

Glossy Skin (Paget).—In some cases of irritative lesion of the sensory nerves of limbs (*e.g.*, from gun-shot), the skin becomes smooth, shiny, sometimes hyperæmic, sometimes œdematous, often superficially inflamed or the seat of sores like chilblains; at the same time the part is often the seat of intense neuralgia. Less severe symptoms, but obviously similar, are seen after simple section, and are due to disturbances of circulation and temperature, and to anæsthesia.

Atrophy of parts cut off from the nervous system. Muscle and certain glands have been treated of above. In the case of muscle, it is to be noted that if it is regularly exercised by the galvanic current, atrophy may long be postponed. In a paralysed limb all tissues ultimately waste; so, also, does the face when paralysis of the facial

is not recovered from. This is due to impaired blood supply, for it occurs in limbs which are simply kept at rest. Atrophy of the cock's comb and turkey's wattles results from section of their nerves, and is perhaps to be similarly explained.

Hypertrophy of bone may follow section of the sciatic in young animals, and is inflammatory; for it never occurs unless large ulcers form, extending to the bone, and even causing necrosis. Hypertrophy of the rabbit's ear after section of its nerves has been said to occur; but many observers have failed to produce it, or have, at most, seen thickening of epidermis and hair upon it.

There is, then, no evidence of the existence of special trophic nerves, and no convincing proof of the interference of the nervous system in the chemical processes of cells which perform no special function. That these processes may go on undisturbed in the absence of nervous influence is shown by the perfect development of other parts which is found in anencephalous and amyelous embryos; by the growth of transplanted epithelium and connective-tissues; and by the union of completely severed parts. At the same time, as we cannot offer a perfect explanation of many of the above-mentioned cases, we cannot say positively that the nervous system has no direct influence upon connective-tissues and epidermic cells. In the present state of our knowledge, however, it is dangerous to explain anything by such an influence; it is better to leave it doubtful.

Having now dealt with the Nutritive and Functional Activities, we must consider the Reproductive. In early life, at least, all cells possess the power of reproducing their like, and in the majority this power is retained, although it may not be exercised physiologically, up to advanced age. Cessation of growth does not imply absence of ability to grow, for growth seems to cease when the supply of nutritive material to a part is only just sufficient to maintain its *status quo*. This is seen in a hair, which will not grow beyond a certain length—

cut it short and growth at once begins again, the supply of food being greater than the now shortened hair requires for simple nutrition. To cause cells, which are capable of multiplying, to do so, the supply of food must be increased. Thus exercise of a muscle causes increased blood-supply and consequent growth; but increased blood-supply to a working tissue, without exercise, will not have this effect. The hyperæmia round an ulcer of the skin causes thickening of epidermis and connective-tissues, and nothing is commoner than new formation of bone round a carious focus. For this effect the increased supply must be very frequent or long-continued.

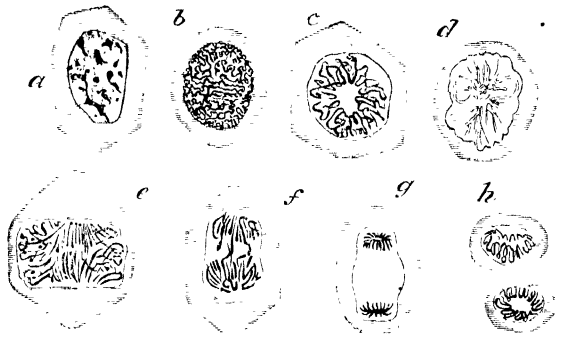
The cells of the body inherit very different amounts of vital energy. The cells of the thymus are soon exhausted, those of the epiphyseal cartilages later, and of the generative organs later still. In all cases, probably, the reproductive activity is the first of the vital manifestations to suffer; then the functional and nutritive. Inability to perform such chemical changes as are necessary to remove effete material and to repair waste is natural in old age; death, which may be termed natural, then results from "senile decay."

GENESIS OF CELLS.—Virchow's dictum—*Omnis cellula e cellula*—is admitted now by all but a few. It may probably be added that every nucleus is derived from a pre-existing nucleus.

Multiplication of cells takes place by **simple division.** The cell divides generally into two; and the change is preceded by remarkable appearances in the nucleus. According to Flemming the process of "karyokinesis" may be very briefly described as follows (Fig. 2):—First, the nuclear membrane disappears; then the **resting** nuclear network (*a*) becomes much finer and closer, like a ravelled **skein**; then again more open, and, if not already so, the cell becomes round (*b*). There seems to be now only one long fibre forming the nuclear network, which next assumes the form of a **rosette** or **wreath** (*c*), round a clear central space, whilst a clear zone intervenes ex-

ternally between the network and the cell-substance proper. By division of the external bends of the fibre, and approximation of the apices of the V's so as to obliterate the central space, a star-form—**aster** (*d*), is produced. The fibres at this stage often become finer and more numerous by longitudinal division from their free ends towards the centre. Instead of radiating from the centre they now become first parallel, and then convergent towards two opposite points—the poles—of the original

FIG. 2.



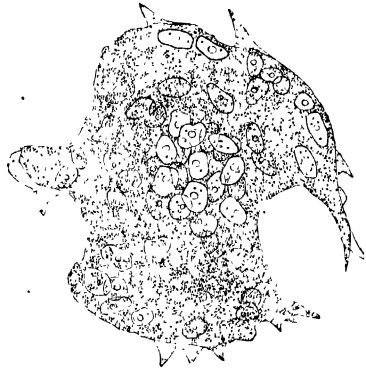
Forms assumed by a nucleus in dividing.—*a*, resting nucleus; *b*, skein-form, open stage; *c*, wreath-form; *d*, aster, or star-form; *e*, equatorial stage of division; *f*, separation more advanced; *g* and *h*, star and wreath forms of daughter nuclei. Reduced from Flemming's drawings in the "Arch. f. Mik. Anat."

nucleus, so that the fibres now form two sets of V's with their angles away from the equator—**equatorial stage** (*e*). A clear equatorial line appears, and widens (*f*), as one set of V-fibres retreats from the other division. From each group the nucleus of a daughter-cell is formed by passing through—in reverse order—all the stages above-mentioned (*g* and *h*), until the resting stage is reached. Meanwhile, the protoplasm of the cell-body collects round each

nucleus, and by the time these have assumed the wreath-form its division is complete. The daughter-cells, at first small, grow, and may themselves shortly divide; and thus multiplication may be very rapid.

The nucleus may divide several times without any division of the cell-body occurring; but the latter increases continuously in size. Thus are produced "giant" or "myeloid" cells—large, irregular, multinucleated masses of protoplasm, which are met with in the marrow of growing bone, in chronic inflammations, and in some new growths. (Fig. 3.)

FIG. 3.



A Multinucleated Cell. From the lung in a case of Chronic Phthisis. Showing the large number of nuclei with bright nucleoli. × 400.

Finally, it remains to be pointed out, that cells originating from one embryonic layer never give rise to cells of a kind formed normally from another layer. **Epiblast** forms nervous tissue, and the epithelium of sense-organs, of the ventricles of the brain and central canal of the cord, of the skin, and of the mouth. **Hypoblast** forms the epithelium of the alimentary canal and of all glands connected with it. The **Mesoblast** forms the epi-

thelium of the kidney, testicle, and ovary; the epithelium of vessels and serous membranes; all the connective-tissues; blood; and muscular tissue.

Having thus dealt with the structure and functions of cells in health, we may now turn our attention to disease. The functions of an organ are really the functions of the cells of which it consists; if all these act normally we say that the organ is sound; and when all the functions of every organ and tissue in the body are normally performed, we describe the individual as being in perfect health. A very little experience shows that physiological functions vary within certain, perhaps rather wide, limits, the perfect well-being of the individual being maintained. Consequently our standard of **Health** is no rigid line; its maximum and minimum are widely separated, and the latter shades off imperceptibly into disease.

It will be inferred from the above that the definition of **Disease** is—*abnormal performance of function by one or more organs or tissues*. This applies to "disease" as a general term; but when we speak of a specific disease, as rheumatism or syphilis, the cause of such disease—that to which the peculiar disturbances of function or structure, which distinguish the disease in question from all others, are due—is implied in the word. The same, or indistinguishable, disturbances of function and structure, may be produced by several causes: it is the more or less constant grouping or sequence of symptoms or lesions which establishes distinct diseases.

It is worthy of note also that the *maintenance of a physiological maximum or minimum* must be regarded as pathological. For example, a man out of training will eliminate much more urea than normal on the first day of a walking tour, but the average daily elimination for the whole tour will not vary from the normal. If, however,

the man were to go on excreting the maximum quantity of the first day, his state would be one of disease.

The complete healthy life of a cell consists in the perfect performance of all its functions. For this, three things are necessary:—1st, that which it inherits—its vital energy—must be normal; 2nd, it must be supplied with sufficient suitable food; 3rd, its surrounding physical conditions must be normal. Failure in any one of these will lead to disease, and two great classes of diseased conditions are at once evident—**inherited**, due to abnormality of the first; **acquired**, due to abnormality of the second and third.

Inherited Disease.—The tendency to inherited disease either exists in the ovum at the commencement of development, or is acquired by the ovum in fertilisation. As in normal development certain organs manifest their inherited tendencies many years after birth, as the development and atrophy of the female generative system at puberty and menopause, the appearance and union of epiphyses, &c.; so inherited tendencies to disease —although like normal tendencies they may appear *in utero*—may not show themselves until late in life, as is the case in cancer of the breast or uterus. It is possible that in many cases the same unrecognised conditions which induced in a parent the morbid tendency handed down, continue to act on the offspring, until—with or without some obvious exciting cause—the disease becomes evident. We cannot say when this tendency to disease begins: it may have been slowly gaining strength for generations. The fact that no progenitor had the disease in question, if he or she lived well past the age at which such disease usually manifests itself, shows simply that the causes had not acted long enough or with sufficient energy to produce it. It is important to recognise that even inherited disease has its starting-point in conditions external to the cells of the body.

With regard to the actual mode in which disease is inherited—it is in some cases probable that the poison, the

actual cause of the disease, is present in the ovum or spermatozoon, as has been shown to be the case in the silkworm disease (Pasteur). But how disease and tendencies to diseases which are not due to any specific poison are handed down, we know no more than we do how it is that children inherit the features of their parents.

Often, no actual disease is inherited, but the power of resistance of certain tissues against the causes of certain diseases (*e.g.*, tubercle) is more or less impaired; or the tissues degenerate early, especially in the fatty or calcareous manner, so that many members of a family may die at about the same age from fatty heart or apoplexy.

Acquired Disease.—Starting with an organism or part the vital energy of which is normal, disease, if it occur, must necessarily be the result of external conditions; the supply of food is faulty either in quantity or quality, or the physical conditions to which the part is, or has been, exposed are unsuitable. It is difficult to separate the two. If the blood-supply to a part is abnormal in quantity, the temperature of the part will be changed; if a portion of the body is mechanically injured, its blood-supply becomes abnormal; if a poison excites fever, the cells are exposed to a higher temperature than normal: a *circulus vitiosus* is established. Disease may be acquired even during intra-uterine life—*e.g.*, acute specifics, syphilis.

General and Local Disease.—Any change in external conditions acting upon a unicellular organism would probably affect every particle of its substance and modify all its functions; all its diseases would therefore be **general.** But multiplication of cells and specialisation of functions enable abnormal conditions to act upon certain groups of cells and to disturb their functions without affecting (primarily, at least), those of other groups. We thus get **local** disease; and the great majority of diseases belong to this class. Perhaps, indeed, we may say that every disease is primarily localised in a tissue or organ—the blood being counted as a tissue of the connective type of which the intercellular substance is fluid.

Structural, Organic, and Functional Disease.—A disease is localised in an organ or tissue during life, by its symptoms and by its physical signs; and after death, we as a rule find the localisation justified by the discovery in the part of some constant structural change. This is **structural** disease. In a large number of cases, however, there are no physical signs, only symptoms (epilepsy), or the physical signs are secondary to some primary abnormality of function in one or more organs (gout, diabetes). There may then be doubt as to the organ or system at fault; and, often, this doubt can be settled only by the discovery of a constant structural change associated with the symptoms in question. Diseases, in which no such change has been found, are classed as **functional**; the belief being that in them the functions of certain cells are abnormally performed, without any structural change. Modern research has greatly diminished the number of functional diseases; but it is almost certain that a very large number of the slighter ailments are due to faults in the chemical changes (the metabolism) effected by cells. **Organic** disease probably, in the first place, meant that pathologists had been enabled to localise a disease in an organ by means of structural change in it. It has now come to be used as synonymous with "structural."

ÆTIOLOGY OF DISEASE.—The causes of disease are divided into two classes—**Predisposing** and **Exciting**.

PREDISPOSING CAUSES.—Any agency which tends to cause departure from the physiological state of the whole body, or of a part, must be regarded as predisposing to disease—*e.g.*, privation, frequent irritation. Many such agencies, when acting more strongly, become excitants of disease—*i.e.*, cause the step outside the physiological limit to be taken. If to ciliated cells, detached from the body and acting strongly under the microscope, a hot iron be approached, its first effect will be to increase or stimulate their action; but if the iron be kept near them long, or be brought closer, their action slows and

ceases. If, now, the iron be removed at once, the cilia will after a period of quiescence begin slowly to work—one here, one there, then all—and may finally recover completely. This was an experiment of Lister, as also was that of showing the resolution of inflammatory stasis in the amputated web of a frog. They illustrate a point of fundamental importance in pathology—*the inherent power of every cell to recover after injury.* They show for the elements what every one knows of the whole—namely, that, *cœteris paribus*, a strong man will recover from a disease which would be fatal to a weakly one. It is certain, too, that the "life" of cells resists the action of injurious agencies; and that this power of resistance varies in the cases of different tissues—*e.g.*, the rabbit's ear resists the effects of anæmia much longer than a knuckle of its intestine; and also in different individuals. Thus, it is a common observation that certain people, who have not suffered from the acute specifics, tend those ill of these diseases without themselves catching them; whilst others again fall victims to them, one after another, *though not specially exposed.* Such power of resisting *certain causes of disease does not imply ability to resist others of a different nature; nor does it necessarily go* with muscular strength. It varies at different times in the same individual.

The following predisposing causes are generally considered:—

Age.—Special treatises have been written on diseases of childhood, and on diseases of old age, showing that there are peculiarities with regard to disease at these periods of life. The special liabilities of childhood are to some extent explained by supposing that the power of resisting injury, which all cells possess, is not fully developed until adult age; those of old age, by the fact that the vital powers are wearing out, and degeneration occurring.

Sex.—The organs special to the sexes render each liable to special diseases. That women are the special victims

of hysteria is probably due to the fact that for generations it has not been considered unwomanly for a woman to display feelings which it has always been the object of men to conceal. But we cannot explain the special liability of women to endemic and exophthalmic goître and myxœdema, nor their comparative immunity from Addison's disease, ataxy, and general paralysis.

Heredity.—It has already been stated that feeble vital power, without actual disease, may be the heritage of the body, or one of its parts. It may be noted further that, like physiological and personal peculiarities, disease sometimes skips one or more generations (atavism)—*e.g.*, gout. In other cases, as in hæmophilia, the disease appears generally in the males only; although the females may, without themselves manifesting it, transmit it to their offspring.

The diseases which most obviously "run in families" are:—functional nervous disorders—hysteria, neuralgia, epilepsy, insanity, and they are more or less interchangeable; carcinoma, especially of the breast and uterus; and some simple growths, especially if multiple (lipomata, osteomata, papillomata); gout, tubercular disease.

Effects of Previous Disease.—Some diseases, when once acquired, tend to recur again and again. This may be because the tissue affected is at the onset incapable of normal resistance; or because, having once been injured by the disease, it does not recover its pristine state. Sir J. Paget points out how exactly the form and structure of a scar are preserved through years; almost as exactly as are those of normal parts which have never been altered by disease. He thinks that this maintenance of the parts in the state to which they have been brought by the injury, accounts for their yielding more and more easily each time they are exposed to the action of the same cause. Catarrhal inflammations of mucous membranes, rheumatism, and facial erysipelas are familiar examples of diseases which tend to recur.

On the other hand, there are several diseases which are

said to be "protective against themselves." An individual who has had small-pox is, for a time at least, not liable to the disease. This, too, Paget explains by supposing that the effect of the disease upon the blood-forming organs is so to modify them that they no longer produce the pabulum necessary for the growth of the small-pox poison. If small-pox be caught a second time, he regards it as a proof that the blood-forming organs have returned to the normal, in accordance with the law above-mentioned—that injured tissues tend to recover.

Certain other diseases, again, seem to modify very deeply the functions of the body. Many years after these illnesses, it is found that diseases, which seem at first sight to have nothing to do with them, yield only to the treatment proper for the original malady. Such are malarial fever, syphilis, gout.

EXCITING CAUSES.—These may all be ranged under the headings of **Abnormal Food-supply** and **Abnormal Physical Conditions.**

Abnormal Food-supply.—This may be due to errors in the circulation or in the composition of the blood. It may result from hyperæmia or anæmia; from all abnormalities in blood-constitution, whether due to faults in its formation or purification, or to the introduction of poisons from without.

Abnormal Physical Conditions.—These include injuries from any one of the physical forces, applied either from without, or, so to speak, from within; the results of mechanical obstacles to discharge of function or of contents—*e.g.*, stricture of a duct or orifice, strangulation of gut, pressure, and the mechanical effects of parasites.

MODE OF EXTENSION OF DISEASE.—**Primary** disease of an organ or tissue is frequently followed by **secondary** disease of other parts. This may happen in several ways:—

1. **By direct spread of a morbid process,** as when in-

flammation extends from skin to subcutaneous tissue, or cancer of the mamma involves skin.

2. **By the carriage of causes of disease from a primary focus to parts at a distance,** by the lymphatics or by the blood-vessels, as in embolism of the most varied substances.

3. **Mechanically,** by so-called "*Back-telling.*" Thus stricture of the urethra causes hypertrophy of the bladder to overcome the obstacle to the outflow of urine, or dilatation of the bladder if its efforts are futile. In either case, the difficulty of entry of urine into the bladder is increased, and the ureters, pelves, and kidneys dilate. Interstitial nephritis results from the pressure, the renal functions are imperfectly performed, and this is detrimental to the organism at large. The succession of changes which result from mitral incompetence is another familiar example of this mode of extension of disease.

4. **Failure of any part to do its share of work in the economy.** The result will depend upon the completeness with which its defection can be compensated. If the work can be done by other parts, as can that of a sweat or sebaceous gland, nothing is noticed; but after extirpation of a kidney which was doing work, a time of danger from diminished excretion of urinary products has to be gone through, the other kidney being at first unequal to the double duty. Failure of the cardiac or of the respiratory function will cause death, there being no power of compensation.

Terminations of Disease.—The possible terminations of disease are recovery, or return of the part to the discharge of its normal functions; partial recovery; and death, or complete cessation of function. Certain diseases can scarcely be said to have a termination; when once established they remain stationary.

CHAPTER I.

NUTRITION ARRESTED.

NECROSIS.

THE absolute and permanent arrest of the performance of function in a part constitutes necrosis, gangrene, or local death.

ETIOLOGY.—Whatever interferes with the supply of nutritive material to a part, or destroys the vital activity of its cellular elements, may cause its death.

A. The supply of nutritive material may be interfered with by :—

1. **Obstruction in the Arteries.**—This is a common cause of necrosis. The obstruction may be caused by compression by ligature, tumour, &c., by rupture, thrombosis, or embolism, or by disease of the arterial coats. If the obstruction be complete and a collateral circulation cannot be established, death of the part quickly ensues.

2. **Obstruction in the Capillaries.**—Obstruction here is often the result of pressure upon or stretching of the vessels. This may take place from the accumulation of inflammatory products, hæmorrhage, or from the pressure exercised by new growths. The resulting obstruction to the capillary circulation causes the death of the immediately adjacent tissues. As examples of necrosis from this cause may be mentioned that of the superficial layers of the bone which so frequently results from periostitis, owing to the compression of the capillaries between the bone and the periosteum ; the sloughing of tendons in whitlows before they are opened ; and the formation of ordinary bed-sores. When inflammation causes gangrene it is ulti-

mately by the production of stasis, leading to death of the tissues from malnutrition and coagulation of blood in their capillaries. Whenever necrosis of a tissue occurs, the blood coagulates in its capillaries; and thus hæmorrhage from gangrenous parts is prevented.

3. **Obstruction in the Veins.**—Obstruction to the return of blood by the veins must be so complete in order to arrest nutrition that it is in itself rarely a cause of necrosis. It is when associated with cardiac weakness or obstruction in the arteries that it constitutes an important agent in producing this result; for then the force necessary to drive the blood on through the much narrowed venous channel is quite inadequate. This is seen after ligature of a main artery and its vein, and in accidental injury of the vein during the operation of ligature of a large artery, especially in the thigh; also in constriction of a part by a bandage not tight enough to occlude the arteries.

4. **Diminished Cardiac Power.**—This is never independently a cause of necrosis. In cases, however, of excessive general debility, or disease of the cardiac substance, the consequent diminution in the contractile power of the heart materially aids the foregoing causes in producing a fatal blood-stasis. The arrest of the circulation in "senile gangrene," and that which so often occurs in the tissues of the back in adynamic fevers and in chronic exhausting diseases, is in part the result of diminished cardiac power. This arrest in the last-named conditions is usually determined by some injurious irritation of the tissue—in other words, it is a part of an inflammatory process.

5. **Inflammation.**—As a cause of necrosis, inflammation belongs partly to group A, and partly to group B. The effect of the inflammatory process is to impede or arrest the circulation, and to impair the vitality of the affected part, and the intensity of the process may be so great as to cause coagulation in the capillaries and death of the tissue (see "Inflammation"). When a strangulated

or invaginated piece of gut is released and the circulation is re-established, severe inflammation, perhaps leading to gangrene, frequently ensues. Cohnheim's experiment of tying off a rabbit's ear has been repeated. It is of practical importance to note that inflammation sets in only on re-establishment of the circulation—*i.e.*, when the gut is returned to the peritoneum; there is none whilst it is in the sac. A much contused and lacerated part may ultimately be killed by the pressure of the effusion from its injured vessels still further impeding the flow through them. Certain inflammations have a special tendency to terminate in necrosis, as diphtheria, carbuncle, noma, "hospital gangrene," and spreading traumatic gangrene. In these conditions the intensity of the injury to the tissues is probably due to the action of minute organisms. In all cases, the more impaired the nutrition of the part which becomes the seat of an inflammatory process, *the more likely is this to cause its death.*

B. Destruction of the activity of the cellular elements may be caused by:—

Physical and Chemical Agencies.—A part may be completely disorganised and lose its vitality as the result of external violence, great heat, or cold. Many corrosive chemicals, as acids and caustic alkalies, destroy the life of cells. Normal urine is very irritating, often exciting extensive sloughing when extravasated from a ruptured urethra. Putrid urine or foul secretions from wounds are even more intensely irritant, sometimes directly destroying the cells like a caustic. As mentioned in the last paragraph, organisms other than those of putrefaction have a similar effect. These physical and chemical causes frequently produce necrosis by exciting, in the first place, acute inflammation.

These are the several causes of necrosis; but it must be borne in mind that the process is often complex, and due to the combined influence of two or more of them. The liability to necrosis will greatly depend also upon *the power of the tissues to resist injury*. This varies,

probably, in different individuals, and, certainly, in different tissues in the same individual—intestine, for example, being much less resistant to injury than skin. Conditions which lead to the death of a part in which the circulation was already impeded, or the vitality of the cellular elements impaired, produce no such effect where such local weakness does not obtain. This is well exemplified by the necrosis of the tissues of the back from pressure, which so often occurs in conditions of debility; by varicose ulcers of the legs; by the gangrene of the extremities which sometimes results from the long-continued ingestion of ergot; and especially by senile gangrene.

Senile Gangrene.—This is a form of necrosis which affects especially the lower extremities of old people, and is the result of several of those etiological conditions which have already been enumerated.

The most important element in the production of senile gangrene is the presence of atheromatous or calcareous changes in the arteries of the limb, which greatly diminish their elasticity and calibre, and proportionately impair the circulation in and nutrition of the part. This is shown by the coldness of feet, cramps, and other abnormal sensations so often experienced by the patient for some time before the gangrene sets in. The slowing of the circulation is usually much increased by simultaneous atrophy or degeneration of the muscular substance of the heart itself. The prolonged contact of the blood with an abnormal vessel-wall, thus brought about, is sometimes sufficient to cause the formation of a thrombus in the artery, which slowly spreads until it may extend from the foot to the groin. Gangrene begins in one or more toes, and also extends slowly. It is surprisingly limited; thus the whole foot may not be gangrenous where the thrombus extends into the popliteal artery. In other cases embolism, with superadded thrombosis, may be the starting-point—a chalky plate or a parietal thrombus being swept from a large into a smaller artery. Finally, the gangrene may be inflammatory, due to some very slight injury, such as

a slight abrasion of the foot, the cutting of a corn, or excess of heat or cold, acting upon the under-nourished vessels and tissues.

THE CHARACTERS OF THE DEAD PART.—These vary according to whether the part dries or remains moist and putrefies. These two varieties are spoken of as **Dry** and **Moist Gangrene.**

Dry Gangrene or **Mummification.**—The conditions favourable to the occurrence of this are:—Causation of the necrosis by interference with the supply of blood to the part, the veins and lymphatics being left free; such position of the part as shall favour the return of fluid by veins and lymphatics; slow progress of the gangrene; removal of the epidermis, which much impedes evaporation; free exposure to a current of cool or hot dry air; and the predominance in the part of such tissues as naturally contain but little fluid—bone, cartilage, and tendon. Under such circumstances the part, which is pale, slowly shrivels, becoming brown or black; and beyond the drying, its tissues undergo little change. Dry gangrene often results from embolism, from slowly progressing arterial thrombosis, and from the prolonged administration of ergot of rye.

Moist Gangrene.—Under opposite circumstances, where, from an acute inflammation, or from venous obstruction combined with a weak arterial supply, a part, consisting largely of muscle and other soft structures, becomes rapidly gangrenous, it is gorged with an albuminous fluid full of breaking-down red blood-corpuscles. The hæmoglobin of these forms a red solution which soaks into and stains all the tissues. The limb is much swollen, of purplish colour, and often studded with bullæ of blood-stained fluid. If such a part is exposed to warm, moist air, septic bacteria quickly enter through the skin, multiply rapidly in the highly putrescible fluid, and generate by their action gases—chiefly sulphuretted hydrogen, ammonia, nitrogen, and carbonic acid—which give rise to the emphysematous crackling so often associated with gan-

grene. The tissues soften and liquefy, the whole part becomes exceedingly offensive, and its tissues change in colour from reddish- to brownish- or greenish-black. For putrefaction to occur it is absolutely essential that the bacterium termo be admitted to the part; consequently such changes are met with chiefly in external parts or internal organs to which air has free access. When the life of an internal organ or part is destroyed, as by infarction, but bacteria are not admitted to it, its tissues undergo a series of degenerative fatty changes known as **necrobiosis**.

COURSE.—Gangrene may be **circumscribed** or **spreading**. The course varies chiefly with the **cause**; but the **resistance of the tissues**, depending upon their vital energy and blood supply, must always be taken into account, for causes which have little effect on healthy tissues lead to sloughing in the aged (p. 28), the diabetic, albuminuric, or intemperate.

With regard to the first factor—circumscribed gangrene implies a circumscribed cause. This form is exemplified by the death of tissue resulting from mechanical violence, the actual cautery, complete stoppage of the circulation, &c. On the other hand, spreading gangrene necessitates a cause which spreads before it. Thus gangrene from arterial thrombosis often spreads, but slowly and with a well-defined margin. But the typical spreading gangrenes are those due to inflammation, in which, probably, the action of organisms on the fluids of the part provide fresh quantities of the irritant.

When the process becomes circumscribed, the dead tissue—sphacelus or slough—acts as an irritant to the adjacent living structures, causing more or less inflammation of them. If the slough is aseptic, the inflammation is slight—leading merely to the formation of a layer of connective-tissue round the dead mass by which it becomes encapsuled. This occurs especially in internal parts, and is best illustrated by the fate of simple infarcts. When thus encapsuled the dead part ceases to

irritate; it becomes decolorised, fatty, infiltrated with small round cells, and is converted into a small fibrous scar, which may calcify.

When the slough is superficial it generally putrefies and becomes strongly irritant; but mummification will prevent this. The inflammation of living tissue round the now limited slough is spoken of as the **line of demarcation.** Exudation and migration occur freely into a narrow zone of *living tissue* surrounding the edges and base of the slough, fibres and all firm connections between the living and dead tissues are softened and eaten through, and, finally, the slough is cast off when this process is complete, by suppuration occurring along the line of demarcation. If the whole thickness of a limb dies, the stump left by casting off the sphacelus will be conical; for the soft parts retract somewhat, and the bone separates lower down. The less vascular a tissue, the longer is the time occupied in its erosion—*e.g.*, fascia, tendon, bone. After removal of the slough, an ulcerated surface is left. If the dead mass be deeply seated, and suppuration occur about it, fistulæ form, leading from it to the surface; through which it may ultimately be cast off. This is seen in necrosis of bone.

POST-MORTEM CHANGES.

The changes which always occur in tissues after death must now be considered more particularly. Firstly, with regard to the blood:—This fluid undergoes the earliest and most rapid change. The hæmoglobin escapes from the red corpuscles, partly by exudation, and partly by the destruction of the corpuscles themselves, and, dissolved in the liquor sanguinis, permeates the surrounding tissues. The corpuscles are ultimately completely annihilated, nothing remaining but a few minute granules. The staining of the tissues with hæmoglobin is commonly known as **post-mortem staining**, and the appearances it presents are very characteristic. The lining membrane of the heart and bloodvessels, being in immediate con-

tact with the blood after death, are the parts principally affected. The staining is of an uniform pinkish-red colour, thus differing from the punctiform and stratiform redness of hyperæmia, from which it must be carefully distinguished. The amount of staining is in proportion to the rapidity with which decomposition has taken place, and to the amount of blood contained in the part at the time of death. Marked staining of the endocardium and great vessels soon after death is a sign of septicæmia.

In muscle the arrest of nutrition is accompanied by a state of rigidity, known as the **Rigor Mortis.** This is a peculiar condition of the muscles observed in almost all bodies after death, in which they become firm and somewhat shortened, as though in a state of chronic contraction. It comes on as soon as the muscles have lost their irritability—*i.e.*, their capability of responding to artificial stimulation; in other words, as soon as the nutritive processes have completely ceased. The time of its appearance will therefore depend upon the state of nutrition of the muscles at the time of death; the more healthy and vigorous this is, the longer it is before the nutritive processes completely cease, and consequently the longer it is before the rigor mortis supervenes. The length of its duration and its intensity are in direct proportion to the lateness of its appearance. In people, for example, who are in perfect health and die suddenly, as from accident, the rigor mortis does not usually come on until from ten to twenty-four hours after death; it is very marked, and often lasts two or three days. In those, on the other hand, who die from some exhausting disease, as from chronic phthisis or the adynamic fevers, in which the nutrition of the muscles becomes much impaired, the rigor mortis appears very soon, sometimes as early as ten minutes after death; it is very slight, and may pass off in less than an hour. It has been said that in cases of death from poisoning by carbonic acid and sulphuretted

hydrogen, from lightning, and from some of the severer forms of the adynamic fevers, the rigor mortis is entirely absent. It is doubtful, however, if this is the case, as the rigor mortis has probably escaped observation, owing to its early supervention and rapid disappearance. As soon as the rigor mortis has passed off, decomposition of the muscular tissue commences.

With regard to the nature of the change, Kühne and others have shown that it is really owing to the coagulation of the albuminous substance of the muscle—myosin. The myosin, fluid during life, coagulates when nutrition has ceased, the coagulation being attended by the liberation of a free acid. Thus are produced the firmness, hardness, and opacity of the muscle characteristic of rigor mortis. These disappear as soon as decomposition commences; the transverse striation of the fibres becomes indistinct, and gives place to irregular rows of granules and fat-molecules, the muscle softens, its sarcolemma is destroyed, and ultimately nothing remains but a soft structureless débris. This change occurs not only in muscle; in the cells of other tissues a similar coagulation of the protoplasm takes place on the cessation of the nutritive processes.

Respecting the *post-mortem* changes in other tissues—protoplasm generally not only coagulates, but tends to become finely granular after death. It sometimes increases in size so that the cells look swollen; and in nucleated cells the nucleus often shrinks or entirely disappears. The cells ultimately break up into molecules of various sizes. In adipose tissue, the cells diminish in size, owing to the escape of the fluid fat, which diffuses itself throughout the surrounding structures. The fibres of connective-tissue swell up, become opaque, and ultimately liquefy. In nerve-fibres, the white substance of Schwann coagulates and collects into small drops (myelin) within the neurilemma. Cartilage and bone resist the putrefactive process longer than any of the tissues, and are the least altered by it.

CHAPTER II.

NUTRITION IMPAIRED.

It has been seen in the preceding chapter that absolute arrest of nutrition is followed by complete cessation of all manifestations of vitality and function, constituting necrosis or local death. Those conditions must now be considered in which the interference with nutrition, for the most part, falls short of absolute arrest, and in which impairment of vital energy is the characteristic, death being only an occasional consequence. Such conditions are comprised under "Atrophy" and "Degeneration."

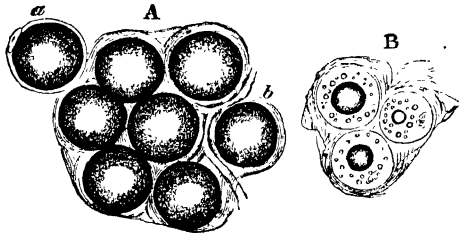
ATROPHY.

Atrophy must be carefully distinguished from arrested development. It is a decrease in the amount of a tissue, owing either to diminution in the **size** or in the **number** of the histological elements of which it is composed. It is attended by loss of weight and impairment of function. When the elements are diminished in size only, it is called **Simple Atrophy**; when the number is diminished it is called **Numerical Atrophy.** These two varieties are often associated, the latter being an advanced stage of the former.

Simple diminution in size of the elements of a tissue is the most common condition met with in atrophy, and may affect all tissues, as is well exemplified by what takes place in ordinary emaciation. Thus, adipose tissue is merely common connective tissue, many cells of which are distended with fat. When a person emaciates, the fat is gradually removed from the cells, so that they diminish in size, and the fat which completely filled the cell may be reduced to a few isolated drops; the cell-wall and nucleus at the same time often become distinctly

visible (Fig. 4). Here there is no destruction of the cells, no diminution in their number, but simply the removal of some of their contents. As the fat is removed from the cells, it is usually partially replaced by a serous fluid. Multiplication of the nucleus is also often observed. The cells of all glands may thus become atrophied, and so

FIG. 4.



Adipose Tissue. A. Normal. B. Atrophic, from a case of phthisis. *a.* A single fat-cell, with cell-wall, nucleus, and drop of fat. × 300. (Virchow.)

produce a diminution in the size of the whole organ. Muscular tissue also may atrophy by simple diminution in the size of its primitive fasiculi; and here, as in adipose tissue, the process appears often to be associated with a multiplication of the nuclei of the muscle. In all these cases the elements remain almost unchanged; hence, all that is necessary for restitution of the tissue is a diminution of waste, or an increase of repair, according as the one or the other is faulty.

A diminution in the number of elements—numerical atrophy—is often an advanced stage of simple atrophy. The elements not only diminish in size, but some of them actually perish and cease to exist as vital agents. It is well seen in advanced atrophies of muscle. In it, restitution is possible only by the production of new elements, whereas in simple atrophy repair can be effected without new formation. In certain tissues, in which growth occurs by addition of new elements, and not by enlarge-

ment of pre-existing cells—as the spleen, lymphatic glands, and skin—atrophy is probably always due mainly to numerical loss.

Atrophy may be **general**—affecting to a greater or less extent all the organs and tissues of the body, or it may be **local** and limited to particular parts. In general atrophy the stress falls at first upon the subcutaneous adipose tissue, then upon the adipose tissue in other situations, as that surrounding the viscera and in the omentum, then upon the muscles and glandular organs, and lastly on the osseous and nervous structures.

Although atrophy in its strict signification consists simply in a diminution in the size or in the number of the component elements of a tissue, it is rarely a perfectly simple process, but is usually associated with more or less **fatty degeneration**. This indicates fault in the chemical processes of the cells. Probably, when the nutrition of a part is so much interfered with as to cause it to atrophy, those portions of its cells, which should be combined with oxygen and rendered soluble, remain; fatty degeneration is the natural fate of protoplasm under such conditions. It is possible, too, that an atrophying tissue would not store sufficient oxygen for its use. It will be seen subsequently that fatty degeneration arises from causes similar to those which produce atrophy itself.

ETIOLOGY.—Atrophy of the whole body or of a part is sure evidence that the total or local nutritive exchange is disturbed so that waste exceeds repair. This is the immediate cause of all atrophies. Repair may be deficient because of insufficient supply of food, or because of inability on the part of the tissues to use the food supplied. The circumstances which excite excessive waste in cells are but little understood (see "Effect of Nervous System upon Nutrition," p. 11). It is convenient to speak of general atrophy as distinct from local.

General Atrophy may be caused by :—

1. **Deficient Supply of Nutritive Material.**—Whatever interferes with the supply of nutritive material to

the tissues will be followed by their atrophy. Deficient supply of food; obstruction to the passage of the food into the stomach or intestines, as in stricture of the œsophagus or pylorus; the mal-assimilation which results from the various conditions giving rise to dyspepsia; interference with the absorption of the chyle, from obstruction of the thoracic duct, or disease of the mesenteric glands constituting the so-called "tabes mesentérica;" may all in this manner be causes of general atrophy.

2. **Excessive Waste.**—All those conditions which are attended by the loss of large quantities of nutritive material may be causes of general atrophy. Such conditions are furnished by continuous hæmorrhages, profuse and long-continued suppuration such as often occurs in caries of the spine and empyema, diarrhœa, and the excretion of large quantities of albumen or sugar, as in Bright's disease or diabetes. The waste resulting from the increased tissue-change which accompanies acute febrile diseases must also be included under this head.

3. **Impaired Vital Activity.**—This constitutes an important element in the production of the atrophy of old age—**senile atrophy**. As life advances, the ability of the elements to perform those chemical processes which are necessary to prepare and assimilate food to compensate for waste gradually diminishes; hence they gradually atrophy, and ultimately all manifestations of their vitality may cease.

Although general atrophy may thus be referred to one of the foregoing causes, it is rarely a simple process, but usually depends upon the combined influence of two or more of them. The atrophy associated with pulmonary phthisis, for example, results partly from the loss of nutritive material in the profuse expectoration and diarrhœa, partly from the deficient supply consequent upon the imperfect oxidation of the blood and upon the interference with assimilation which is so often caused by structural changes in the stomach and intestines, and partly from the increased tissue-change of fever. In

senile atrophy, again, in addition to the general diminution of nutritive activity, there is frequently some condition of the digestive organs interfering with assimilation which materially aids in producing the ultimate result. Increased tissue-waste, loss of appetite, and interference with assimilation are all causes in the production of the atrophy which accompanies fever.

Local Atrophy.—In dealing with local atrophy, it is much more difficult to discover which of the factors in the nutritive exchange is at fault. The first group is a simple one.

1. **Deficient Supply of Nutritive Material.**—The effect of diminishing the blood-supply to a part will vary with the amount of diminution from slight atrophy to death.

Diminished supply of arterial blood is a common cause of atrophy, and may be brought about in various ways. (1.) By obstruction of the supplying vessels before they enter a part; thus atrophy of the testis may result from pressure of an abdominal aneurism on its artery, and wasting of the proximal fragment of a long bone may follow its fracture above the point of entry of the nutrient artery. (2.) Pressure may be continuously exercised upon a part, in such a way as not to constrict the veins specially; thus is produced atrophy, even of bones, from pressure of aneurisms and tumours, deep fissures in organs like the liver by pressure of band-like adhesions, atrophy of kidney from obstruction in urinary passages, and, rarely, wasting of a testis by pressure of old hæmatoceles or hydroceles. (3.) Pressure may be developed within the capsule of an organ by the appearance of some new growth, or of some inflammatory effusion—especially that of small round cells going on to the formation of young, strongly contractile connective-tissue. The effect of this is seen in granular contracted kidney, cirrhosis of the liver, and indeed in all "sclerosing" processes. In groups (2) and (3) the pressure must also act directly on the cells of the part and so impair their powers. These groups

include the atrophies commonly known as **pressure-atrophies.**

2. **Diminished Functional Activity.**—This is a convenient clinical group, many examples occurring both physiologically and pathologically. But diminished function is never more than the remote cause of atrophy, the immediate, being either deficient supply of food or impaired vital energy.

Diminished functional activity of a part means that the chemical processes going on in its cells are less active than normal, and such cells will require less food. The means by which the needs of each tissue are made known to the blood-forming organs is not understood; but the supply is, as a rule, speedily adapted to any variation in their wants. Consequently, working tissues will, soon after they have ceased to perform their functions, receive only sufficient material for those chemical processes which do still go on in them. This is insufficient to maintain the mass of protoplasm required to do the full work of the tissue; so some of it atrophies.

After birth, those parts which are no longer required in the altered circulation gradually atrophy. The umbilical arteries and vein become thrombosed up to their first branches, and shrink to a fibrous cord as the clots organise. But this does not explain the closure of the Ductus venosus or D. arteriosus, in which the conditions are not favourable to thrombosis. Obliteration of these vessels can at present be spoken of simply as a developmental fact, comparable to closure of the foramen ovale. The thymus disappears in the second year; the female generative apparatus atrophies at from forty-five to fifty, the male somewhat later; the spleen and whole lymphatic system waste after middle life. Probably in these cases the vital energy of the cells of the parts concerned is exhausted about the times mentioned, and diminished function is the result—not the cause. They would then be of the same nature as senile decay.

Thus, muscles rendered inactive by ankylosis or

chronic disease of joints, by splints, or by paralysis from disease or injury above the anterior cornual cells with which they are connected, atrophy. When the muscles of a part waste, all its other tissues—nerves, vessels, bones, &c.—suffer ultimately from impaired blood-supply. Thus, in part at least, we may explain wasting of the bone in a stump or in a limb long kept at rest; the absence of that intermittent pressure, which it is the function of bones to bear, is probably a secondary cause. The rectum dwindles after colotomy to a scarcely pervious cord; in addition to the loss of muscular action, no doubt, passage of fæces over the mucous membrane acts as a stimulant to its vessels, and, as it is never distended, the tissues adapt themselves to the empty condition. Atrophy of the optic nerve follows on removal of the eyeball.

But when a muscle is cut off from its connection with its cells in the anterior cornu, or when these cells are destroyed or seriously injured, an atrophy of the muscle, which is much more rapid than that resulting from diminished functional activity, sets in. In the latter case, those changes which nervous stimuli alone can physiologically excite, probably go on (p. 9); but in the former they are completely arrested. Examples of this atrophy are afforded by the acute bulbar and spinal paralysis of adults, infantile paralysis, some cases of progressive muscular atrophy, neuritis from any cause, rupture, contusion, or section of a nerve. Certain glands (salivary, testis?) waste on section of their nerves. Nerves cut off from their ganglion cells also degenerate rapidly, and waste. These are spoken of as **trophoneuroses** (see p. 8). In all of these the interstitial connective-tissue increases, and often becomes loaded with fat as the higher tissue disappears.

3. **Excessive Functional Activity.**—This may, quite exceptionally, be a cause of atrophy—*e.g.*, of testis. (See also "Hypertrophy of Muscle," p. 113).

PHYSICAL CHARACTERS.—The estimation of

atrophy is often a matter of considerable difficulty. The great criterion is diminution in absolute weight. The weight of an organ, however, varies considerably in health; it varies with the weight of the body as a whole, and it may be less than natural from incomplete development. The same is true also of the muscular and osseous systems. An accumulation of blood and serosity in an organ may again increase its weight, and thus constitute a source of fallacy. This is often the case in organs which have been for some time mechanically congested, in which, although their size and weight may be increased, their tissue is considerably diminished in amount.

Organs which are atrophied are usually diminished not only in weight, but also in size. In most cases they contain less blood, they are drier, firmer, and more fibrous in consistence than in health. Their functional powers are invariably diminished. The whole of the textures of which an organ is composed may suffer; some, however, usually do so more than others. The fibrous constituents are the last to atrophy; hence the firmness, toughness, and loss of elasticity so commonly met with in the atrophied parts. In glandular organs, the secreting cells are usually the first to show signs of atrophy; they become smaller, and are often finely granular, from the presence of molecular fat; the vessels and nerves also share in the wasting process. In the subcutaneous cellular tissue, the fat is gradually removed from the cells, which thus diminish in size. In muscles the primitive fasciculi become smaller, and their transverse striæ gradually disappear; ultimately the whole of the contents of the sarcolemma may be entirely removed, and nothing remains but the connective tissue. This process is usually accompanied by more or less fatty degeneration of the muscular fibres, and in some cases by the development of fat between the fasciculi. (See "Fatty Infiltration of Muscle.")

ATROPHY OF BONE.

Atrophy of bone is always attended by a diminution in weight, but not always by a diminution in size. It is met with in two forms. In one, the compact and cancellous tissue gradually become absorbed, the medullary canal diminishes in size, and the whole bone thus becomes smaller. This is known as **concentric atrophy.** It is met with especially in the long bones in cases of long-standing anchylosis, dislocations, or paralysis.

In the other variety of atrophy there is no diminution in the size of the bone, but merely a gradual conversion of compact into cancellous tissue. The whole bone thus becomes rarefied, and it is exceedingly light and brittle, so that it fractures with great facility. This, in contradistinction to the former variety, is known as **eccentric atrophy.** It is usually met with as a senile change, and is in most cases accompanied by more or less fatty degeneration.

PULMONARY VESICULAR EMPHYSEMA.

This appears to be the proper place to describe the changes met with in the lungs in emphysema, inasmuch as these changes are characterised mainly by atrophy of the walls of the air-vesicles.

Emphysema consists essentially in a permanent enlargement of the infundibula and air-vesicles in larger or smaller areas of the lungs. The dilatation appears usually to commence in the infundibulum, and to extend from this to the air-vesicles which open into it, so that ultimately the whole may be thrown into one large cavity. As the process proceeds, communications are established between adjacent groups of air-vesicles, and thus cavities of still larger area are produced.

Atrophous Emphysema.—The more minute histological changes which accompany emphysema vary somewhat in different varieties of the disease. In that form

of emphysema which occurs in old people, and which is essentially a senile change, the alterations in the walls of the air-vesicles consist simply of atrophy of the several structures of which they are composed:—hence the term **atrophous** or **small-lunged** emphysema, which is applied by Sir W. Jenner to this variety of the disease. The air-vesicles may not be much increased in size, but several of them are thrown into one, their walls are considerably thinner than natural, the connective-tissue, elastic-tissue, and bloodvessels all having apparently shared in the wasting process. There is usually also an abnormal amount of pigmentation. Such lungs are smaller than natural, and quickly collapse when the thorax is opened.

Hypertrophous Emphysema.—In the other important variety of emphysema the lungs are increased in size, so that they often bulge forwards when the thorax is opened, and in contradistinction to the former variety, certain constituents of the lung-tissue appear to be increased in amount, inasmuch as the lungs are less crepitant, and feel somewhat denser and tougher than natural. This is described by Sir W. Jenner as **hypertrophous** or **large-lunged** emphysema.

When such lungs are examined microscopically, it will be found that the dilatation of the air-vesicles is more marked than in atrophous emphysema, although less general in its distribution. The atrophic changes also do not affect equally the various tissues which make up the alveolar walls. The elastic fibres appear to be more especially wasted, whilst, according to some observers, the connective-tissue is increased. I have been unable to discover any marked increase of the connective-tissue in the alveolar walls, although an increase of this tissue is often to be seen around the smaller interlobular bloodvessels and bronchi. The capillary bloodvessels which are distributed on the walls of the air-vesicles are atrophied and diminished in calibre, owing to the stretching and pressure which result from the vesicular dilatation, whilst the larger interlobular vessels are often found thickened

and distended with blood. In some cases there is more or less fatty degeneration of the epithelium, and usually an abnormal pigmentation of the lung.

ETIOLOGY.—It would be beyond the scope of the present work to discuss the various theories which have been propounded to account for the development of emphysema. It is, however, obvious that all conditions which increase the pressure on the inside of the air-vesicles, or damage the resisting powers of their walls, may be causes of permanent vesicular dilatation.

Increased pressure on the inside of the air-vesicles may result from—

1st. Violent expiratory efforts with closed glottis, such as occur during the act of coughing, blowing wind instruments, violent muscular exertion, &c. Those parts of the lungs which are least supported will be over-distended. This is the expiratory theory of Jenner.

2nd. Certain portions of the lungs being incapable of expansion, owing to collapse, consolidation, asthmatic spasm, &c. There will be excessive tension in those parts into which the air can enter.

Impairment of the resisting power of the air-vesicles may result from—

1st. The loss of elasticity and atrophy which is a concomitant of old age. This is the most important element in the causation of atrophous emphysema.

2nd. The atrophy of the air-vesicles resulting from that stretching of their walls and obliteration of their blood-vessels which is caused by their over-distension from increased pressure exercised upon their inner surface.

3rd. Damage to the walls of the air-vesicles resulting from inherited weakness, or due to some interference with their nutrition from mode of life or other causes.

DEGENERATION.

The "Degenerations" include a class of morbid processes which are characterised by an alteration in the

quality of the tissues, and which, like atrophy, are attended by impairment of function, and often by annihilation of histological elements.

Atrophy and degeneration are both steps towards death. In atrophy, however, as pointed out by Virchow, nutrition is simply altered in **quantity**; the waste of the tissue is in excess of the assimilation of new material, and, consequently, there is a diminution in the amount of the tissue and an impairment of its functional powers. In degeneration, on the other hand, nutrition is altered in **quality**—the metabolism of the cell is abnormal; an abnormal substance exists in the tissues, which is either formed by metamorphosis of their protoplasm, or is brought to and deposited in the tissue, and is not consumed. This is attended by impairment of the vitality and functions of the elements of which the tissue is composed, resulting either from the presence of the new material, or dependent upon the same conditions as those which gave rise to its formation.

ETIOLOGY.—Of the causes of the Degenerations as a class but little can be said, the various forms depending for the most part upon different conditions. These will be considered under their respective heads. Our knowledge of this class of morbid processes is necessarily very incomplete, inasmuch as so little is known of the chemical changes which take place within cells. (See p. 7.)

The Degenerations may be divided into two classes—the **Metamorphoses** and the **Infiltrations.**

1. **The Metamorphoses.**—These are characterised by *the direct metamorphosis of the albuminoid constituents of the tissues into a new material. This is usually followed by the destruction of the histological elements and the softening of the intercellular substance, so that ultimately all trace of structure may be lost, and the* function be completely arrested. The Metamorphoses include Fatty, Mucoid, Colloid, and probably Lardaceous Degeneration.

2. **The Infiltrations.**—These differ from the Metamorphoses inasmuch as the new material which exists in the tissues is not derived from their albuminoid constituents, but is deposited in them from the blood; there is an infiltration and deposition of a new substance. This is rarely followed by destruction of the histological elements, or by softening of the intercellular substance; hence the structure of the tissue is much less altered than in the Metamorphoses, and function is usually much less interfered with. The Infiltrations include Fatty, Calcareous, and Pigmentary Infiltration.

CHAPTER III.

FATTY DEGENERATION.

FATTY DEGENERATION is an abnormal accumulation of fat in the tissues. An accumulation of fat occurs, however under very different circumstances, and under the general term of "fatty degeneration" are included different pathological processes. Before proceeding to describe these processes and the histological changes which they produce, it will be well to consider, in the first place, the sources from which the fat met with in the body is derived; and secondly, the circumstances under which it may accumulate so as to constitute a morbid process.

General Pathology of Fatty Degeneration.—The chief source of the fat met with in the body is the oleaginous constituents of the food. A portion of these are stored up in the cells of certain tissues, to be utilised as producers of force and heat when the requirements of the system may demand it. The cells of adipose tissue, those of the medulla of bone, and to a less extent, those

of the liver, thus serve as physiological reservoirs for fat.

The other sources from which fat may be derived is from saccharine and albuminous principles. The albuminous principles in the process of nutrition undergo decomposition, and the products of their decomposition contain a certain amount of fat. This is usually completely removed by oxidation, but under certain circumstances the oxidation is incomplete, and the fat accumulates in the cells of the tissue.

In considering the circumstances under which an accumulation of fat in the tissues may constitute a morbid process, it is to be remarked that it often becomes exceedingly difficult here to draw any sharp line of demarcation between health and disease. This is especially the case when the accumulation of fat is excessive in situations where fat is normally met with. When it occurs in abnormal situations the morbid nature of the process is evident.

An accumulation of fat in the tissues may occur so as to constitute a morbid process under the four following conditions:—

1st. When the food contains an excess of fat, or of substances capable of becoming converted into fat. Under such circumstances the oxygen taken into the body is insufficient to oxidise the excess, and it consequently accumulates in the cells.

An accumulation of fat from this cause occurs as a physiological process in the growth of adipose tissue. Adipose tissue is a connective-tissue containing numerous cells which are distended with fat. The growth of this tissue thus consists simply in the fatty infiltration of more of these cells. (Fig. 5.) If this be excessive it constitutes obesity. The temporary accumulation of fat in the liver during the digestion of an aliment rich in fatty substances is another example of this kind of deposition. This will be described when speaking of the "fatty liver." If the amount of fat be very great it may accumulate, not only

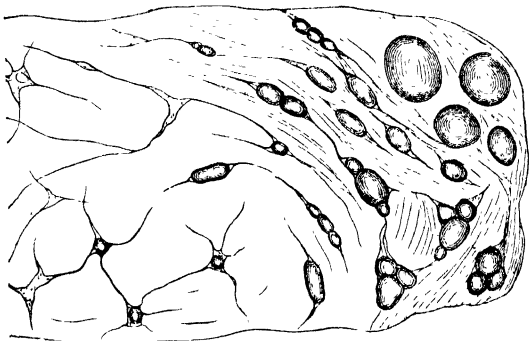
in normal situations, but also in tissues where fat is not usually met with, and in both cases the accumulation will thus constitute a morbid process.

2nd. When there is no such excess of fatty substances in the food, but the processes of oxidation are so imperfectly performed, either locally or generally, that the fat contained in a natural diet is incompletely oxidised.

3rd. When the fat which is liberated from the nitrogenous constituents of the food during the process of nutrition does not undergo the complete oxidation which it should, and so remains within the cells.

4th. When the fat which is liberated from the protoplasm of cells during the progress of nutrition is incompletely oxidised, and so accumulates in, and takes the

FIG. 5.



Fatty Infiltration of Connective-tissue. Showing the accumulation of fat within the cells. × 300 (Rindfleisch).

place of, the protoplasm. Here there is a gradual replacement of the protoplasm by molecular fat, so that the cell ultimately may be completely destroyed.

Fatty degeneration in which there is this destruction of histological elements is one of the most common forms of the disease, and it will hereafter be more fully described

as **fatty metamorphosis**. Its nature was first pointed out by Dr. Quain in his well-known researches on fatty degeneration of the heart.* Dr. Quain then stated that the fat met with in the muscular fibres in this condition was the result of a metamorphosis of the fibres themselves, and was not derived from without. The truth of Dr. Quain's teaching has since been confirmed by the experimental investigations of Drs. Voit and Bauer.

Voit and Bauer's investigations were made with the object of determining the source of the fat in that acute form of fatty degeneration which is produced by poisoning with phosphorus, in which the degeneration is due mainly to a diminution in the oxidising power of the blood, caused probably by the destruction of the red-blood cells.† They gave phosphorus to dogs which had for some days previously been starved, so that any fat which might be present in the tissues after death could not have been derived either from the food or from the adipose tissue of the animals. The phosphorus produced very extensive and general fatty degeneration, and the fat must obviously have arisen from the protoplasm of the cells. Voit concludes from these investigations—1st. That the transformation of albumin which takes place in cells is independent of the supply of oxygen, but that if the oxygen be deficient, the fat and other products of the transformation, being incompletely oxidised, accumulate in the cell. 2nd. That the presence of fat in the cells may thus be due to increased transformation of the albumin, or to diminished oxidation of the products of its decomposition. 3rd. That the fatty degeneration in poisoning by phosphorus is due both to an increased transformation of the albumin of the cells, and to *diminished oxidation of the fat and other products of the transformation.*

* "Medico-Chirurgical Trans. Lond.," 1850, vol. xxxiii.

† Voit and Bauer, "Zeitschrift für Biologie," vii. pp. 63–85; and Voit, "Neues Repertorium für Pharmacie," xx. pp. 340–349.

It will thus be seen that of the four conditions enumerated as causes of fatty degeneration, in all, with the exception of the first, the accumulation of the fat is principally due to incomplete oxidation, whilst in the first there is no imperfection in the oxidising processes, but the oxidisable materials are in excess. These two conditions are frequently associated.

Incompleteness of oxidation, and a consequent tendency to the production of fat, occurs under various circumstances. The red blood cells being the carriers of oxygen, all those conditions in which the supply of blood is interfered with, the red blood cells diminished in number or defective in quality, or the oxygenation of the blood imperfectly performed, may lead to fatty degeneration.

Interference with the supply of blood to a part, and consequent fatty degeneration from imperfect oxidation, may result from narrowing of the nutrient bloodvessels. This is seen in the heart as the result of atheromatous changes in the coronary arteries, and in organs in which the lumen of the vessels is diminished by lardaceous or syphilitic changes. The interference with the supply of blood caused by inflammation and mechanical congestion in the same way leads to fatty degeneration. Organs and tissues which have been long disused, and in which, consequently the quantity of blood circulating through them and the oxidation processes become diminished, undergo fatty changes (see "Fatty Infiltration of Muscle"); as do also the cancers and other rapidly-growing tumours in which the rapidity of growth is out of proportion to the vascular supply.

An alteration in the blood as a whole, and a consequent general tendency to fatty changes, is seen in chlorosis and in those conditions of anæmia which are sometimes produced by chronic and acute diseases; also in the fatty degeneration which results from poisoning by phosphorus. The long-continued abuse of alcohol, and the influence of a high temperature, by diminishing

the absorption of oxygen by the tissues, tend to produce fatty changes. The senile forms of fatty degeneration, which affect especially the cornea and cartilage, are due to that diminution in the activity of the circulation which exists in old age. Lastly, the imperfect oxygenation of the blood which results from chronic diseases of the lungs constitutes an important element in the causation of the fatty degeneration which so frequently exists in these diseases.

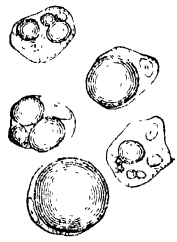
In proceeding to consider the histological changes which are produced in the tissues by an accumulation of fat, it is in the first place to be remarked that in those cases in which the fat is derived from the food, it is, for the most part, deposited in those situations in which fat is normally met with; whereas when it originates in the tissues it may occur in the cells of any part. The changes produced in the tissues must obviously vary in the two cases. Where the fat is derived from the metamorphosis of the nitrogenous constituents of cells the process is accompanied by more or less destruction of the cell, and by a corresponding impairment of its functional powers —the tissues are destroyed in the process; whilst in the other cases no such destruction usually takes place. Although these two conditions may occasionally be associated, yet, owing to the marked difference in the results which they respectively produce, it will be well to speak of them separately; that in which the fat is derived from the metamorphosis of the tissues being termed **Fatty Metamorphosis**; that in which it is derived from the oleaginous, saccharine, or nitrogenous principles of the food, **Fatty Infiltration.**

FATTY INFILTRATION.

In Fatty Infiltration, the fat which is deposited within the cells usually occurs as distinct drops of oil. In the earliest stages of the process these are very small, but as the deposition proceeds they gradually accumulate

and run together, displacing and obscuring the nucleus and protoplasm, until the cell is completely filled and distended with oil. (Fig. 6.) The vitality and functions of the cells are but little impaired by the accumulation, and the protoplasm—although rendered almost invisible when this is excessive—remains unaltered. The cells within which the fat accumulates not being destroyed, the removal of the fat is all that is necessary to restore them to their original condition. As already stated, fatty infiltration occurs as a physiological process in the growth of adipose tissue, and also in the liver during the digestion of an aliment rich in fatty substances.

FIG. 6.



Liver Cells in various stages of Fatty Infiltration. × 300 (Rindfleisch).

FATTY INFILTRATION OF MUSCLE.

In muscle, fatty infiltration is frequently met with as a morbid process. The cells in the connective tissue which surrounds the fasciculi of the muscle become filled with fat; and this development of fat between the primitive muscular fasciculi has often been confounded with degeneration of the fibres themselves. In this latter process, however, which will subsequently be described as **fatty metamorphosis** of muscle, there is a direct metamorphosis of the muscular fibres into fat; whereas in the condition now under consideration, there is a deposition of fat *between* the fasciculi, which remain—during the early stages, at all events—unaffected. The interstitial fat varies in amount. In some cases single rows of fat cells alternate with rows of muscular fasciculi; at other times the accumulation is less regular, more existing between some fibres than between others: in all cases, however, the muscular elements may be discovered lying amongst

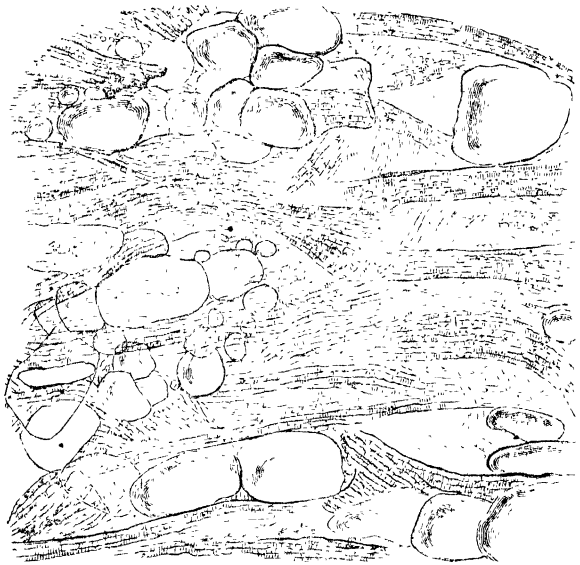
the fat. (Fig. 7.) If the latter be very considerable in amount, the muscle may appear to the naked eye to be entirely converted into fat; but the microscope will always reveal the muscular structure in which it is embedded.

This condition is frequently met with in animals which have been fattened, the fat increasing not only in the usual situations, but also accumulating between the fasciculi of the muscles. In muscles also which from any cause have for some time been incapacited, and in which consequently the circulation of blood and the oxidation processes are reduced to a minimum, this interstitial growth is extremely liable to occur—*ex. gr.*, in the extensors of the wrist-joint in cases of lead-poisoning, and in long-standing paralysis from lesions of the brain or cord, also in muscles which have been rendered useless by anchylosis of a joint. In progressive muscular atrophy, as Virchow has shown, the affected muscles exhibit this change, together with true fatty metamorphosis.

Fatty Infiltration of the Heart.—In the heart fatty *infiltration is not unfrequently met with; and here it is especially important to distinguish it from the much* more grave condition in which the fibres themselves are primarily affected. In health, there is a varying amount of fat covering the surface of the heart beneath the visceral layer of the pericardium, which is always most abundant in the grooves between the auricles and ventricles, where it surrounds the blood-vessels. This may increase so as to completely envelop the organ, and at the same time gradually insinuate itself between the muscular fibres, so that to the naked eye all appearance of muscular structure may be lost, the walls looking like a mass of fat. In hearts less affected, striæ of fat will be seen lying amongst the muscle. (See Fig. 7.) The fat is always most abundant near the surface, the muscular structure becoming more evident towards the endocardium.

The immediate effect of the interstitial growth is to displace and compress the muscular fibres between which it insinuates itself, and in doing so it diminishes the contractile power of the muscle. This is especially important when occurring in the heart. The pressure, however, which it exercises upon the fibres and the accompanying

FIG. 7.



Fatty Infiltration of Heart. A section from the more external portion of the left ventricle of the heart, showing the growth of fat *between* the muscular fibres. The fibres are in some places atrophied and commencing to undergo fatty metamorphosis. × 200.

blood-vessels, ultimately causes atrophic and degenerative changes. Thus the fasciculi gradually atrophy, the transverse striation becomes indistinct and is replaced by molecular fat; in fine, true metamorphosis of the muscle is established. These two processes, indeed, not uncom-

monly go hand in hand together, the interstitial infiltration preceding the intrastitial metamorphosis.

FATTY INFILTRATION OF THE LIVER.

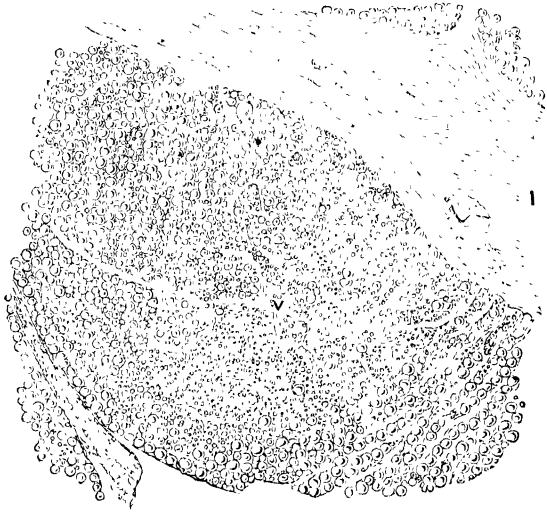
In the liver fatty infiltration is exceedingly frequent, constituting what is commonly known as the "fatty liver." The hepatic cells always contain a small quantity of fat, which is temporarily increased after the ingestion of fatty substances. It will be well to describe this physiological infiltration before proceeding to the morbid process.

The ingestion of an aliment rich in fatty substances is followed by a temporary excess of fat in the portal blood, and by the deposition and temporary accumulation of a portion of this within the hepatic cells. This fat is first deposited in the cells which are in immediate contact with the capillaries of the portal vein, and thus is produced an excess of fat in the cells at the circumference of the hepatic lobules. This gradually passes from the cells at the circumference to those in the interior, whence it is ultimately conveyed again into the circulation. This process goes on until the excess of fat is removed from the blood, when the hepatic cells again acquire their former character. There is thus a transitory accumulation of fat within the hepatic cells which is gradually removed, the vitality of the cells not being thereby impaired.

The morbidly fatty liver is one which contains an abnormal quantity of fat, and here also, as the fat is usually deposited from the blood in the portal capillaries, the increase is first observable in the external zone of the hepatic lobules. (Fig. 8.) It accumulates here within the cells as minute globules, which as they increase coalesce and form large drops of fat. These ultimately completely fill and distend the cells, which at the same time become larger and more globular in shape. (See Fig. 6.) As the process proceeds, the accumulation

advances from the periphery towards the centre of the lobule, until its whole mass may be involved, and the cells universally become distended with fat. The vitality of the cells is not materially impaired by the infiltration; they continue to perform their functions, as is shown by the presence of bile in the stools and in the gall-bladder.

FIG. 8.



Fatty Liver. Showing the accumulation of fat in those cells more especially which are situated in the external zone of the lobule. There is also some increase in the interlobular connective-tissue (Cirrhosis). V. Hepatic vein. 1. Interlobular connective-tissue. × 50.

In some exceptional cases the accumulation of fat is most marked around the hepatic vein. This, according to Virchow, is probably to be explained by supposing that the fat is becoming excreted, and that only the last cells retain a little of it.

The fatty liver is somewhat increased in size, in advanced stages often considerably so. The surface is smooth, the edges are thickened and rounded, the specific gravity is diminished, although the absolute weight may be increased, If the infiltration be slight, involving merely the portal zone of the lobules, the cut surface will present a mottled appearance, the external fatty zone being of an opaque yellowish-white colour, whilst the central portion remains unaltered, or is perhaps somewhat hyperæmic. The more extensive the infiltration the larger is the pale zone, and ultimately, when the whole lobule is involved, there may be left in the centre merely a reddish-brown point, which corresponds with the commencement of the hepatic vein; and in many cases even this point is lost. The organ is then of an almost uniform opaque yellowish-white colour, and the boundary between the individual lobules may be completely obscured. In exceptional cases the accumulation of fat is much more abundant in some portions of the liver than in others, so that on section yellowish points and streaks are seen scattered over its surface. The consistence of the organ is much diminished, it feels doughy, and pits on pressure with the finger, and the knife used to cut it becomes coated with oil. The pressure exercised by the infiltrated fat produces considerable anæmia of the organ, but the interference with the circulation is never sufficient to cause ascites, hæmorrhage, or other evidences of portal congestion.

The liver is especially liable to become the seat of fatty accumulation. This, as shown by the late Dr. Bence Jones, is owing—firstly, to the excess of non-nitrogenous oxidisible matter in the portal blood; secondly, to the deoxidised condition of the portal blood; and thirdly, to the low pressure and slowness of circulation in the portal vessels—conditions the least favourable to oxidation.*

* "Lectures on Pathology and Therapeutics." Dr. Bence Jones, p. 179.

An accumulation of fat in the liver occurs under two opposite conditions—one in which there is general obesity, and the fat accumulates in the liver in common with other parts; and another, in which there is general emaciation, and a consequent impairment of the oxygenating power of the blood. The fatty infiltration of the liver which is so constantly associated with certain chronic diseases of the lungs, is also partly due to imperfect oxygenation of the blood from destruction of lung-tissue. Fatty liver caused by phosphorus and other poisons has been already alluded to.

The other variety of fatty degeneration—fatty metamorphosis—will be described in the following chapter.

CHAPTER IV.

FATTY DEGENERATION (*continued*).

FATTY METAMORPHOSIS.

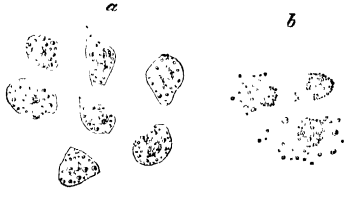
This differs from fatty infiltration, inasmuch as the fat is derived from the albuminous constituents of the tissues themselves, and not from the fatty, saccharine, or nitrogenous principles of the food.

The process consists in the gradual replacement of the protoplasm of cells by molecular fat, in the manner described in the preceding chapter. The fat makes its appearance as minute granules and molecules, usually first in the protoplasm, and subsequently in the nucleus. The granules—which are characterised by their dark colour, sharp contour, strong refractive power, and solubility in ether—gradually increase in number, and ultimately the whole of the protoplasm may be transformed. As they increase some of them may coalesce, and so form distinct drops of fat. As the process pro-

ceeds the cells undergo an increase in size and become more globular in shape, the nucleus becomes involved, *the cell-wall, when this exists, is destroyed, and the cell may thus be converted into a mass of granular fat.* (Fig. 9.)

These granules of fat sometimes remain for some time in a coherent form, and they then constitute what were formerly known as the "inflammatory" or "exudation corpuscles," or "corpuscles of Gluge," which are so common in chronic cerebral softening, and in some other forms of fatty degeneration. (Fig. 9, *b*.) Ultimately the albuminous matter between the granules of fat liquefies, the corpuscles break up, and the fat becomes distributed in the tissue. (Fig. 9, *b*). These granular corpuscles will be more fully considered when speaking of cerebral softening.

FIG. 9.



Fatty Metamorphosis of Cells. *a*. From a cancer. *b*. From the brain in chronic softening. The latter show the large "granular corpuscles," and also the manner in which these become disintegrated. × 200.

Types of this pathological process are furnished by many well-known physiological ones, one of the most characteristic of which is perhaps the secretion of milk. The secretion of milk takes place in the following manner:—The mammary gland becomes exceedingly vascular, white blood-corpuscles escape from the vessels, the epithelium multiplies, and a large number of young cells thus make their appearance in the ducts of the gland. These cells as they are produced become converted into

fat, the cells break up, and the fatty matters in a more or less coherent form constitute the milk-corpuscles. In the earliest stages of the process the granules of fat cohere and form the colostrum-corpuscles, which are precisely analogous to the large granular corpuscles met with in chronic cerebral softening, &c. (Fig. 9, *b*); but as the secretion becomes fully established, and the disintegration of the cells takes place more rapidly, the fatty molecules become at once distributed in the liquid in which they are suspended, giving to the secretion its characteristic white colour. The milk-corpuscles thus formed are replaced continuously by new cells, which in their turn undergo fatty metamorphosis, and in this manner a continuous formation and destruction of cells take place. Other examples of fatty metamorphosis are afforded by the formation of the sebaceous matter of the skin, the cerumen of the ears, and the corpus luteum in the ovary; all of which take place in the same way by the fatty metamorphosis and destruction of newly formed cells.

The immediate effect of fatty metamorphosis is to produce more or less softening of the affected part, and necessarily to impair or annihilate function. If large tracts of tissue are affected, the change is readily recognisable by the diminution in consistence and elasticity which are produced, and in many cases also by the opaque yellowish-white colour. If, however, the change is limited to minute portions of the tissue, its existence can only be discovered with the aid of the microscope.

The fatty particles into which the cells have been transformed are, under favourable circumstances, readily absorbed. The fat may thus be removed and the degenerative process cease before the part has been dangerously involved. Such recovery probably often occurs, for example, in the kidneys and heart. When the elements are completely degenerated the fatty débris is also usually removed by absorption. This is seen in the fatty degeneration and absorption of inflammatory products,

such as occurs in croupous pneumonia. In order for such absorption to take place it is necessary that the tissue should be freely supplied with blood-vessels. If this is not the case, the degenerated products are liable to undergo certain changes whereby they become converted into a pultaceous crumbling material somewhat resembling cheese:—this is known as **caseation.**

CASEATION.—This is a modification of the degenerative process in which the fatty products gradually dry up into a yellowish friable material, which has been compared to soft cheese. This change appears to be owing to a natural dryness of the degenerated tissue, resulting from deficient vascular supply. It is most frequent in parts which contain but few vessels, or in those in which these become obliterated by inflammatory products or by some new growth. Growths composed of closely-crowded cells—as epithelial accumulations within the pulmonary alveoli, growths in the lymphatic glands, in the brain, and in osseous structures, are the most liable to become caseous.

The process consists in a gradual drying up of the degenerated elements; the fluids are absorbed, the cells —which are many of them incompletely degenerated—shrivel and atrophy, the fat undergoes partial saponification, cholesterine forms, and the tissue thus becomes converted into a soft, yellowish-white, cheesy substance, composed of atrophied cells, fatty débris, and cholesterine crystals. This material may gradually dry up more and more, and ultimately become encapsuled by a layer of fibrous tissue.

These cheesy matters are constantly met with, especially in the lungs, and considerable confusion has arisen as to their nature and origin in this situation. This has proceeded from its having been formerly the custom to look upon all cheesy masses as essentially tubercular. Tubercle, it is true, often undergoes, to a greater or less extent, fatty degeneration, and it may thus, like all other growths which have undergone this process, become converted into a yellow cheesy substance; but it

is by no means true that all cheesy masses are tubercular. The pathological significance of caseation is thus less limited than was formerly supposed, and although this change is undoubtedly most common in tuberculous and scrofulous lesions, its occurrence merely indicates that the elements have undergone fatty metamorphosis, and under no circumstances is it in itself evidence of any one particular form of morbid growth. (See "Scrofulous Inflammation.")

The caseous mass may subsequently become calcified, or undergo a process of softening and liquefaction.

CALCIFICATION.—This is an advanced stage of the preceding process. It most frequently occurs in those cases in which the caseous mass is completely enclosed and isolated from the external air, as when in the lymphatic glands, in bone, or when encapsuled in the lungs. The mass becomes infiltrated with calcareous particles, and is thus converted into a calcareous concretion. (See "Calcareous Degeneration.")

SOFTENING.—This process consists in a liquefaction of the caseous substance, which is probably owing to some chemical change in its constituents. It most commonly occurs in parts which come into contact with the external air, especially in those situated in the lungs. The caseous mass liquefies, and is converted into a thin puriform liquid, containing curd-like cheesy matter, which to the naked eye looks much like pus, but under the microscope is seen to consist simply of granular débris, fat, and cholesterine crystals. This, if not discharged, may, like the caseous masses, ultimately dry up and become calcified.

FATTY DEGENERATION OF ARTERIES.

Fatty degeneration of arteries may be a primary or secondary affection. As a secondary process it is met with in atheroma and other inflammatory conditions of

the vessels, in which the fatty change is preceded by a cellular infiltration of the sub-endothelial connective-tissue. (See "Atheroma.")

Primary fatty degeneration is a passive process, not being preceded by any increased nutritive activity of the parts affected by it. It may affect both the internal, middle, and external coats of the artery, but it is most common in the first-named situation. The change usually commences in the endothelium and the connective-tissue cells in the most internal layers of the inner coat, small groups of cells becoming affected in various parts of the vessel; and it may gradually extend from within outwards, the intercellular substance softening, until, in exceptional cases, the whole thickness of the intima is destroyed. (Fig. 10.)

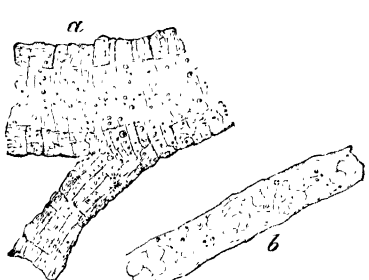
FIG. 10.

Fatty Degeneration of the Internal Coat of the Aorta. Small yellowish-white patches scattered over the lining membrane of the vessel. A very thin layer peeled off and × 200, showing the groups of fat molecules, and the distribution of fat in the intima.

In the earlier stages of the process the condition is recognised by the existence of small, irregular-shaped patches of an opaque yellowish-white colour, projecting very slightly above the surface of the intima. These, which are so constantly met with on the lining membrane of the aorta, may at first be mistaken for atheroma.

They are in most cases, however, readily distinguishable by their superficiality, and by the facility with which they can be stripped off from the subjacent layers, which present a natural appearance. In atheroma, on the other hand—which affects the deeper structures—if the superficial layer be removed, the opacity and thickening are seen to exist beneath it. In many cases the change is limited entirely to the innermost layers of the vessel; the more the subjacent tissues are involved, the greater is the irregularity in the shape of the patches, and the less readily can they be separated with the forceps. The opaque patches occasionally break down, the cells are destroyed, the intercellular substance softens, and the granular débris is carried away by the circulation, leaving small, irregular, superficial erosions upon the lining membrane of the vessel. These erosions are not ulcers in the true sense of that term, not being the result of an active process. They resemble the superficial erosions so common upon the mucous membrane of the stomach, as described by Dr. Wilson Fox.

FIG. 11.



Fatty Degeneration of small Vessels of Pia Mater. From a case of chronic Bright's Disease. *a.* A small artery, the coats of which are somewhat thickened. *b.* A capillary, in which are seen a few red blood-corpuscles. × 400.

Simple fatty degeneration may occur in any of the arteries, but it is in the smaller ones that its injurious influence is most marked, and in these it is more especially liable to affect the external coat. (Fig. 11.) Here, by diminishing the elasticity and contractility of the vessels, it causes degenerative changes in the parts which they supply, and often leads to rupture. This is exemplified by many cases of chronic cerebral softening and cerebral hæmorrhage, although here atheromatous are often associated with the fatty changes. In the larger arteries, as the aorta—where it is exceedingly common—it is of less importance, the inflammatory process, atheroma, having here a far more deleterious effect.

FATTY DEGENERATION OF CAPILLARIES.—The capillaries may also be the seat of fatty changes. Here they are most common in the nervous centres, and in the kidneys in Bright's disease. (See Fig. 11, *b*.) The process commences in the endothelial cells, and may involve considerable areas of the capillary wall, so that rupture is often the ultimate result. This is common in the smallest cerebral blood-vessels, where it is sometimes a cause of cerebral (capillary) hæmorrhage.

Primary fatty degeneration of blood-vessels is in most cases a senile change; it is an expression of that general impairment of vitality which exists in advanced life, and is usually associated with similar changes in other parts. When, however, it is limited to the lining membrane of the largest arteries it is often met with in early life and in persons who are otherwise perfectly healthy. Fatty degeneration secondary to inflammatory conditions will be considered subsequently. (See "Inflammation of Blood-vessels.")

FATTY DEGENERATION OF MUSCLE.

Both striated and non-striated muscle may be the seat of fatty degeneration. In the latter, the muscular fibre-cells are the seat of the change; they become filled with

fat granules and are ultimately destroyed. This condition is frequently met with in the middle coat of arteries which are undergoing fatty degeneration.

FIG. 12.

Fatty Degeneration of Muscular Fibres of Heart. *a.* Earlier stage. *b.* More advanced. × 400.

In striated muscle—both in the voluntary and in the involuntary of the heart—the fibres themselves are the seat of the morbid process, which consists in the replacement of the albuminous matter, of which the fibre is composed, by fat. The earliest stage of the affection is characterised by an indistinctness in the transverse markings of the fibres, which in many parts become studded with minute particles of fat. (Fig. 12.) These gradually increase in number and size, and are usually distributed somewhat irregularly within the sarcolemma. In some parts single rows of granules are found running along the length of the fibre; in others, they are grouped around the nuclei or arranged in transverse lines corresponding with the striæ of the muscle. The fibres become extremely friable, and are readily broken up into short fragments. As the process proceeds the transverse markings entirely disappear, and nothing but molecular fat and oil globules are seen within the sarcolemma. The sarcolemma itself may ultimately be destroyed, and nothing remain of the original fibre but the fatty débris into which its albuminous constituents have been converted. This is true fatty degeneration of muscle; in it the muscular elements are destroyed, and it thus differs essentially from fatty **infiltration,** in which there is simply a development of fat between the fasciculi, the fasciculi themselves not being primarily affected. (See "Fatty Infiltration of Muscle.")

FATTY DEGENERATION OF THE HEART.

It is in the heart that fatty degeneration of muscle is most frequently met with, and here it assumes a most important aspect from the deleterious influence which it exercises upon the motor power of the organ. The muscular substance may be affected throughout, or the degeneration may be confined to certain portions of it. The wider the extent of tissue that is affected, the less advanced, as a rule, is the degree of the degeneration. It is in those cases in which small tracts of tissue only are involved that the process is met with in its most advanced stage.

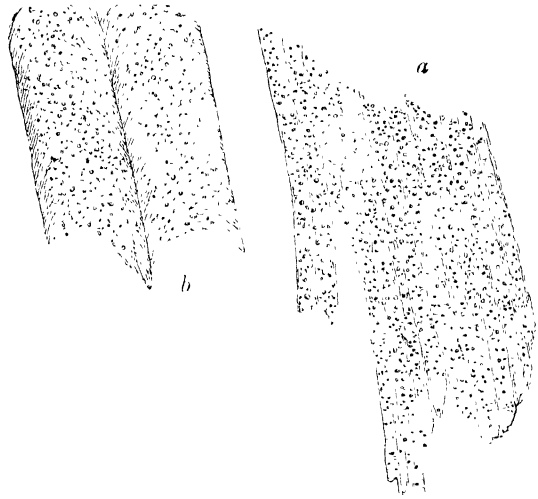
When the change is slight and more or less general, the muscle is somewhat softer and more flabby than natural; it is more friable, and often breaks with a soft granular fracture; and its colour is rather paler and more opaque than that of healthy cardiac tissue. Under the microscope the muscular fibres are seen to have lost to some extent their striated appearance, and to contain granules of fat. (Fig. 12, *a*.)

This diffuse form of degeneration may occur in the course of those diseases in which the oxidation processes are reduced to a minimum; in all those diseases, in short, which are attended by marked anæmia, whether this anæmia be gradually or rapidly induced. In the case from which the accompanying drawing was taken the degeneration was acute. (Fig. 13.) This was the case of a weakly young girl who was under my care suffering from slight valvular disease. She quickly succumbed with acute fatty degeneration of the heart and other muscles, which was induced by a profuse loss of blood during a menstrual period, and by inability to retain food.* Interference with the circulation in the coronary arteries is also a frequent cause of a more or less general

* This case is reported in "Trans. Clinical Society, London," vol. viii. 1875.

degeneration of the muscular tissue. This occurs especially as a result of aortic incompetence, and explains the early failure of cardiac power in this form of valvular disease. Atheromatous changes in these arteries, such as result from the increased blood-pressure of Bright's disease, lead in the same way to fatty degeneration. Lastly,

FIG. 13.



Acute Fatty Degeneration of Heart and of other Muscles. *a*. Heart. *b*. Rectus abdominis. The whole of the heart-tissue was affected, and also the muscles in other parts of the body. × 400.

in its slightest degrees, a diffuse fatty degeneration of the heart sometimes occurs in the course of acute febrile diseases. This will be again referred to in the chapter treating of the histological changes produced by pyrexia.

Sometimes the degeneration, although perhaps more or less general, is much more advanced in some parts than in others. In such cases the heart presents a mottled appearance; opaque pale yellowish or brownish patches

are seen irregularly distributed throughout its substance. These patches, which vary considerably in size and form, are met with especially in the papillary muscles, the columnæ carneæ, and in the layers of fibres immediately beneath the endocardium. They may also occur beneath the pericardium, and in the deeper portions of the organ. They correspond with the most degenerated portions of the tissue. They are soft and flabby, and have a rotten consistence, tearing readily under the finger. Under the microscope, the fibres are seen to be in an advanced stage of fatty degeneration, their sarcolemma containing molecules of fat and oil globules, which in many parts have escaped and lie free amongst the surrounding less degenerated tissues. (Fig. 12, *b*.) These more localised degenerations are most common in old people, and usually result from considerable disease of some branches of the coronary blood-vessels, and not from conditions of general anæmia. The peripheral layers of muscular tissue also frequently undergo extensive fatty degeneration as the result of pericarditis. The connection between these localised degenerations and rupture and aneurism of the heart is well known.

FIG. 14.

Brown Atrophy of the Heart. Showing the granules of pigment and the atrophy of the fibres. The latter have in some parts undergone slight fatty metamorphosis. × 400.

BROWN ATROPHY OF THE HEART.—Somewhat allied to, and occasionally associated with, fatty degeneration of the heart, is the condition known as brown atrophy. This consists in a gradual atrophy of the muscular fibres, together with the formation of granules of brownish-yellow or blackish pigment. These granules of pigment, which are probably the colouring matter of the muscle, are either grouped in clusters around the nuclei, or more generally distributed within the fibre. The fibres are frequently, at the same time, the seat of more or less fatty degeneration. (Fig. 14.) This

change usually occurs as a senile one, or as a part of general marasmus from other causes. It is also met with in some cases of cardiac hypertrophy. Its recognition is in most cases impossible without the aid of the microscope.

FATTY DEGENERATION OF THE KIDNEYS.

Fatty degeneration of the kidneys frequently occurs as a result of inflammation of the organs. This **secondary** degeneration will be alluded to when treating of renal inflammations. Primary fatty degeneration is much less frequent. It must be borne in mind that the renal epithelium very commonly contains more or less fat; but it is only when this is excessive that it can be regarded as a diseased condition. This excessive formation of fat in the kidney is, I think, less common than is generally supposed. It is, however, occasionally met with in chronic diseases, especially in pulmonary phthisis. It is also a result of poisoning by phosphorus.

In simple fatty degeneration, the change is usually confined to the epithelium of the cortex. The cortex presents on section a somewhat yellowish-white surface, often slightly mottled, and this, in most cases, is most marked near the bases of the pyramids. There is no adhesion of the capsule or granulation of the surface. This change appears to interfere but little, if any, with the functions of the organs, and in this respect it resembles the analogous change in the liver. It is not usually accompanied by albuminuria.

CEREBRAL SOFTENING.

This is, perhaps, the most suitable place to speak of cerebral softening, inasmuch as fatty degeneration of the brain-tissue usually constitutes a prominent feature in the histological changes. Softening of the cerebral substance is essentially a necrotic process, and may result from all those conditions which interfere with vascular

supply. The portions of the brain which are the seat of this change may be merely rather softer than the surrounding healthy tissue, breaking down more readily under a stream of water which is allowed to fall upon them—or they may be completely diffluent. They are never distinctly circumscribed, but pass by insensible gradations into the neighbouring tissue.

Under the microscope, the change is seen to consist in a disintegration of the nerve-tissue. The white substance of the fibres first coagulates, then breaks up into masses of various sizes (myeline), and these usually undergo more

FIG. 15.

Chronic White Softening of the Brain.—Showing the granular corpuscles, broken-down nerve-fibres, and fat granules, of which the softened substance is composed. One or two nucleated cells (probably nerve-cells) are also visible. × 250.

or less fatty metamorphosis. The cells of the neuroglia, the small blood-vessels, and, when the grey matter is implicated, the large nerve-cells, are also involved in the necrotic change. The tissue is thus converted into broken-down fibres, granular matter, and molecular fat, and amongst this are numbers of the large granular corpuscles already alluded to (Fig. 15). These corpuscles, as previously stated, although formerly looked upon as the result of inflammation, appear to be simply conglomerations of granular matter resulting from the degeneration of cellular elements (see Fig. 9), and in

the brain, where they are much the most common, many of the granules are probably myeline and not fat. These corpuscles are exceedingly characteristic of cerebral softening. They vary in size from $\frac{1}{500}$ to $\frac{1}{2000}$ inch in diameter, and originate, according to Virchow and Robin, from the cells of the neuroglia—the connective tissue of the brain. The small arteries and capillaries running through the softened part are many of them filled with granules and granular cells, the latter probably originating in the white blood-corpuscles which have accumulated in the part and undergone fatty changes. As the process proceeds, the cerebral substance is completely destroyed, and all trace of nerve-structure is ultimately lost.*

The colour of the softened portion varies considerably. It may resemble that of the surrounding healthy tissue, or be of a yellowish or reddish tint. According to these variations in colour, cerebral softenings have been classified into **white, yellow,** and **red.** The colour depends in great measure upon the amount of blood contained in the part, and on this account is important, as indicating the manner in which the softening has been brought about.

White Softening.—This is, in the great majority of cases, a chronic process. It occurs especially in old people, and is here usually due to that disease of the smaller cerebral blood-vessels and consequent interference with the circulation which is common as a result of age. The impairment of the contractile power of the heart must also constitute an auxiliary in the causation of the imperfect vascular supply. The change in the inner coat of the cerebral arteries due to syphilis is another cause of this form of softening (see "Syphilis"). It is the gradual manner in which the supply of blood is diminished which accounts for the absence of hyperæmia or hæmorrhage, so

* According to Prof. Cohnheim the granular corpuscles are white blood-cells impregnated with fatty or other particles derived from the surrounding degenerated tissue.—*Vorlesungen ueber Allg. Pathologie*, Band 1.

that the colour of the softened portion either resembles that of healthy brain-tissue, or is an opaque dirty white. White softening is sometimes acute, in which case it is usually due to the sudden obstruction of the circulation by the impaction of an embolus in one of the larger arteries. (See "Embolism of the Brain.")

Yellow Softening.—This is, in most cases, simply a variety of the former process, in which, from the fine state of division and close aggregation of the granular matter, a dead yellowish-white colour is imparted to the softening tissue. This colour is probably often partly owing to the presence of altered blood pigments, the result of some previous slight extravasation. The pigment may sometimes be seen as fine dark granules, scattered through the cells of the neuroglia and the nerve-cells of the grey matter, where at first sight they look like fatty particles: they are distinguished, however, by their dark black colour. A softening of the brain more rapidly induced, as by embolism or thrombosis, may also occasionally be of a yellow colour. This, however, is only the case when the softened portion has attained a certain age, and much of the extravasated blood has been removed by absorption. Lastly, a condition of gelatinous œdema of a yellow colour, which has been described by Rokitansky as often being present in the immediate vicinity of cerebral tumours, has been regarded as a variety of yellow softening.

Red Softening.—This is commonly a more acute affection, most frequently dependent upon vascular obstruction, either from embolism or thrombosis. There is collateral hyperæmia, rupture of capillaries, and extravasation of blood; the softened tissue is consequently of a deep red colour. These forms of softening will be described in the chapter on "Embolism." Red softening is also sometimes associated with the chronic white variety, some of the diseased vessels giving way, and thus extravasation of blood taking place into the already softened tissue. Lastly, red softening may be inflammatory. (See "Inflammation of the Brain.")

CHAPTER V.

MUCOID AND COLLOID DEGENERATION.

UNDER this head is included a class of morbid changes which are characterised by a peculiar softening of the tissues. Colloid and mucoid degeneration have frequently been described under the common term of "colloid softenings," but, although they are closely allied and sometimes associated, they appear to constitute two distinct processes.

MUCOID DEGENERATION.—This consists in the transformation of the albuminoid constituents of the tissues into **mucin,** owing to which they become converted into a material of a soft, mucilaginous, jelly-like consistence. This is the condition of nearly all tissues in their immature or fœtal state: the connective tissues in the fœtus consist almost entirely of this soft mucin-yielding substance. Some tissues retain these characters after birth. The umbilical cord, and the vitreous humour of the eye, are both composed of this substance.

A mucoid change occurs as a physiological process in the secretion of mucus. The newly-formed cells undergo mucoid transformation, which results in their destruction, and the mucus is thus liberated; or the cells may evacuate the mucus without being destroyed. This process occurs much more rapidly in all catarrhal conditions of the mucous membrane.

Mucin is closely allied to albumen, more so than to either gelatin or chondrin: it differs from it in not containing sulphur. Like albumen, it is only met with in alkaline fluids—being held in solution by the free alkali—from which it is precipitated by dilute acetic acid. It

differs from albumen in being insoluble in an excess of the acid, and also in not being precipitated by boiling, by tannin, or by bichloride of mercury. Its behaviour with these two reagents will also distinguish it from gelatin and chondrin, which are both precipitated by them.

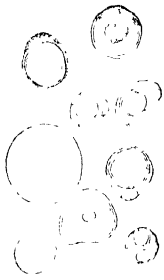
As a pathological process mucoid degeneration may also affect both the cells and the intercellular substance. It is met with in catarrh of mucous membranes, and in epithelial cells in other situations; also in connective tissue, cartilage, especially the intervertebral and costal cartilages of old people, in bone, and in many of the new formations. Wherever it occurs it produces softening of the affected parts; which are transformed into a homogeneous, colourless material, of a soft mucilaginous jelly-like consistence. If the change is limited to isolated portions of the tissue, the softened parts surrounded by those which are unaltered, often present the appearance of cysts. These cyst-like formations containing mucoid substance are not uncommonly met with in the costal cartilages and in new growths.

As to the cause of the mucoid change, nothing is known.

COLLOID DEGENERATION.—This is allied to the former, inasmuch as it consists in a metamorphosis of the albuminoid constituents of the cells. The substance into which the protoplasm is transformed is known as **colloid** material. Colloid closely resembles mucin, but it differs from it chemically, in containing sulphur, and in not being precipitated by acetic acid. It is a colourless, transparent, glistening material of the consistence of jelly or half-set glue. It makes its appearance within the cells as small lumps, which gradually increase in size, pushing the nucleus to one side, until they completely fill the cell. (Fig. 16.) The cells are thus destroyed, and converted into colloid masses. The small colloid masses subsequently swell up, coalesce, and so form larger masses of firm, transparent, yellowish, jelly-like material,

which are readily to be recognised by the naked eye. As the colloid matter increases, and the cells are destroyed, the intercellular substance atrophies or softens, and in this way cyst-like cavities are formed, within which is contained the gelatinous substance. Here it may subsequently undergo a process of liquefaction. (See Fig. 61).

Fig. 16.



Colloid Cells, from a colloid cancer (Rindfleisch.)

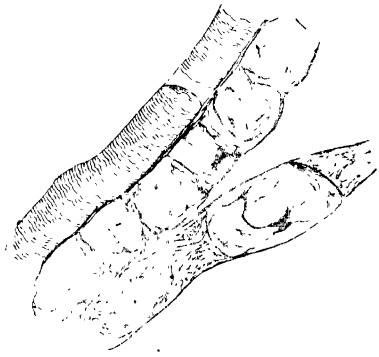
The colloid change is most common in enlargements of the thyroid gland, in the lymphatic glands, in the choroid plexus, and in many of the new formations. (See "Colloid Cancer.") Its causes and nature are as obscure as those of the allied mucoid softening.

It is when occurring in new formations that these two forms of degeneration assume their most important aspects. Certain varieties of tumours may originate as mucoid or colloid growths, or may subsequently undergo these morbid transformations. The mucous tumours (myxomata), which resemble in structure the umbilical cord, consist entirely of a gelatinous mucin-yielding substance. The sarcomata, lipomata, enchondromata, and the cancers may also become the seats of these forms of softening. Such growths have sometimes been described as gelatiniform or colloid **cancers,** this term having been applied to them without any regard to their structure or real nature. Cancers, it is true, may undergo a colloid change (see "Colloid Cancer"); but it is by no means true that all tumours possessing these soft gelatiniform characters are cancers. The terms "mucoid" or "colloid" applied to a new growth merely imply certain physical and chemical characters, and convey but little information as to its real nature.

ZENKER'S DEGENERATION OF MUSCLE.

Allusion must be made here to a change met with in the muscles in typhoid fever, and occurring under certain other conditions, which was first described by Zenker, and which has been supposed to be somewhat allied to colloid degeneration. This change, when occurring in typhoid, is most marked in the recti muscles of the abdomen, the adductors of the thigh, and in the diaphragm. The portions of muscle affected are more opaque than natural,

FIG. 17.



A Portion of the Soleus Muscle from a Case of Typhoid Fever. Preparation teased after treatment with Müller's Fluid. × 200. Reduced ⅓.

of a reddish-grey or brownish-yellow colour, and abnormally friable. Under the microscope, the altered fibres are much swollen, the transverse striation is lost, and the sarcolemma is occupied by a homogeneous, structureless material. This material is exceedingly brittle, and, as usually seen, presents a wrinkled appearance, or is broken up transversely into several irregular fragments. (Fig. 17.) The fibres are never universally affected, but many normal are associated with altered elements. This change necessarily impairs the contractile power of the muscle,

and it often leads to rupture of some of the fasciculi and hæmorrhage. The new material appears to be readily absorbed, and the lost fibres to be quickly regenerated.

With regard to the nature of the change, but little is known. Although most frequent in typhoid, it occurs occasionally in other severe febrile diseases. It is also described by Cornil and Ranvier as sometimes occurring in muscles in the neighbourhood of abscesses, of inflamed bone, and of tumours. Muscles which have been bruised or otherwise injured, whether before or after systemic death, occasionally exhibit a similar change; and Prof. Cohnheim considers that it is probably merely some disturbed form of post-mortem coagulation of the muscle. Whether this be so, or whether the change is due to some abnormal chemical process taking place in the muscle during life, must in the present state of our knowledge remain uncertain.

CHAPTER VI.

LARDACEOUS DEGENERATION.

LARDACEOUS degeneration, which is one of the most important of the degenerative processes, is an alteration in the tissues characterised by the appearance in them of a peculiar homogeneous translucent substance closely allied to albumen, by which their vitality becomes diminished and their functions impaired. It is often known as the **amyloid** change, this name having been applied to it by Virchow, from the supposed resemblance of the new material to cellulose or starch. The term lardaceous originated in the fact that the affected organs have somewhat the appearance of lard or wax, and as being that by which it is perhaps most generally known, it is here adopted.

This form of degeneration is very rarely a primary affection, but almost invariably occurs as the sequel of some other disease. There are two conditions which appear to be especially concerned in its causation—suppuration and syphilis. It is in those diseases which are attended by profuse and long-continued suppuration, such as chronic diseases of bone, empyema, chronic disintegrative diseases of the lungs, chronic pyelitis, and chronic intestinal ulceration, that the lardaceous change is most frequently met with. It also occurs in the advanced stages of syphilis, but especially in those cases in which there is chronic bone disease or chronic ulceration. In quite exceptional cases it is met with in the absence of either of these conditions.

Nearly every organ and tissue may be the seat of the change; those, however, in which it is especially prone to occur are the **liver,** the **spleen,** the **lymphatic glands,** the **kidneys,** and the **intestines.** It is met with less frequently in the stomach, in the supra-renal capsules, in the pharynx, the œsophagus, in the bladder, prostate, and generative organs, in serous membranes, in the membranes of the brain and cord, and in muscle. It also occasionally affects pathological products, as thrombi, inflammatory exudations, &c. It is rarely limited to one organ, but several organs are almost invariably simultaneously affected by it.

Respecting the nature of the new material which exists in the tissues, the analyses of Kekulé and Schmidt show that it is a nitrogenous substance closely allied to albumen. The conclusions arrived at by these observers are, however, not satisfactory, as they were unable completely to separate the substance from the tissues. More recently, Kühne succeeded in more completely isolating it. He submitted the affected organs to a process of artificial digestion, and inasmuch as the lardaceous substance is not dissolved by digestion with pepsin, it was thus obtained free from the tissues in which it was contained. The result of Kühne's analyses is very

similar to those of Kekulé and Schmidt. Dr. Dickinson regards the new substance as fibrin deprived of its alkaline salts. The investigations of Dr. Marcet* show that the affected organs are considerably deficient in potash and phosphoric acid, whilst they contain an excess of soda and chlorine. In conclusion it may be stated that although the precise composition of the lardaceous substance has not yet been determined, the results of the several analyses appear to justify the opinion that it is some modification of albumen.

The most characteristic feature of the lardaceous substance is the peculiar reaction which it gives with iodine, and with iodine and sulphuric acid. If an aqueous solution of iodine—made with the help of potassium iodide—be applied to a lardaceous organ, the affected portion changes to a deep reddish-brown colour. This is not permanent, but gradually passes off, and the part regains its former appearance. If the application of the iodine be followed by the cautious addition of sulphuric acid, a blackish-blue or violet tint is produced. This latter reaction, however, is not easily obtained, considerable nicety being required in the application of the reagents. The following is the method for obtaining it, recommended by Professor Virchow:—A dilute aqueous solution of iodine must be allowed to soak well into the tissue, the excess must be poured off, and a single drop of concentrated sulphuric acid gradually added, when a blue or violet colour will be produced, either at once or after some time. In the hands of English pathologists this latter reaction has certainly met with but little success; and if the colour be obtained, it is by no means satisfactory, and more nearly resembles a black than the blue which has been described. Fortunately, however, the reaction with iodine alone is sufficiently characteristic, and the attempt to obtain the blue by the subsequent

* See "Report of Committee on Lardaceous Disease," *Trans. Path. Soc. Lond.* 1871.

addition of sulphuric acid, is therefore quite unnecessary. If the change is at all advanced, the reddish-brown colour will be produced by merely pouring the aqueous solution of iodine over the cut surface of the organ; but in slighter degrees of the affection, thin sections must be made with a Valentin's knife, and well washed with water to remove the blood, before the coloration with iodine can be obtained.

Certain other forms of altered albumen exhibit a similar colour when treated with iodine, so that this reaction cannot be regarded as absolutely characteristic. Recently M. Cornil has discovered another property of the lardaceous substance, which consists in the deep violet red staining which it undergoes when treated with a solution of methylaniline violet, the healthy tissue being coloured an indigo blue. This reaction appears to be valuable, inasmuch as the staining is much more permanent than that caused by iodine, and thus is more suited for microscopical purposes; and as the iodine reaction can be obtained with other albuminous bodies, M. Cornil's method is especially valuable as a confirmatory test.

The lardaceous substance usually makes its appearance first in the small arteries, the cells of the intima and of the muscular coat being first affected, then the remaining structures of the artery. When the vessels have become involved the new material appears in the immediately surrounding parts, both in the cells and in the intercellular substance. The change may thus involve the whole organ, or it may be limited to certain portions. In the spleen, for example, it is frequently limited to the Malpighian corpuscles; and in the liver to the cells in the more immediate vicinity of the hepatic artery.

The alterations produced in the tissues by this degeneration are very characteristic. The cells gradually increase in size, they lose any irregularities in their contour, and become rounder and more regular in shape, their nuclei disappear, and the whole cell is converted into a structure-

less homogeneous body which has a peculiar translucent glistening appearance. (Fig. 18, *a*.) If the cells are in close contact many of them may coalesce, and their distinctive boundaries thus become obliterated. (Fig. 18, *b*.) The intercellular substance in the same way acquires a homogeneous glistening appearance. The walls of the

FIG. 18.

Lardaceous Liver Cells. *a*, Single cells. *b*. Cells which have coalesced. × 300. (Rindfleisch.)

small arteries—in which, as already stated, the change usually commences—become considerably thickened, the cells of the muscular coat enlarge and ultimately coalesce, the calibre of the vessel becomes diminished, and the circulation through it is consequently impeded. (See Fig. 20.)

Organs in which this change is at all advanced present features so characteristic that its nature can be readily recognised by the naked eye. They are usually considerably increased in size; their absolute weight is increased, and also their specific gravity; their surface is smooth, and the capsule tense and stretched; their consistence is firm and somewhat elastic. On section they exhibit a peculiar homogeneous, glistening, translucent appearance, somewhat resembling wax or glue. Owing to the diminished calibre of their blood-vessels, and to the pressure exercised by the new material, they contain but little blood, and hence are always pale in colour. Although the above characters are often sufficiently marked, they should always be confirmed by the application of iodine or methylaniline to the cut surface of the organ. In slighter

degrees of the affection, when the physical characters are but little altered, the application of these reagents may become necessary in order to discover the presence of the new substance.

The effect of lardaceous degeneration is to impair or even to completely destroy the nutrition and function of those organs which are affected by it. This is owing to two causes—the obstruction offered to the circulation, and the injurious influence of the new material upon the vitality of the affected cells. The obstruction to the circulation, which results partly from the diminution in the calibre of the small arteries, and partly from the general pressure exercised by the new substance, causes an insufficiency in the supply of arterial blood. As a consequence of this, the cells tend to undergo fatty metamorphosis, which indeed is frequently associated with the lardaceous change. As this form of degeneration is almost invariably secondary to some grave constitutional state, it can rarely be looked upon as in itself a cause of death, although it may materially hasten, and even determine, the fatal termination.

Having thus described the nature of the lardaceous substance, and the way in which it makes its appearance in the several tissues of an organ, it remains to consider the source from which it is derived. The disease has usually been regarded as an infiltration, as the deposition in the tissues of some new material derived from the blood. This view is based upon the way in which the several tissues of an organ are affected, the change usually commencing in the small nutrient blood-vessels, and extending from them to the surrounding parts; upon the general character of the affection, several organs being simultaneously involved; and upon the fact that the disease is almost invariably secondary to chronic suppuration or syphilis. The existence, however, of any albuminoid substance in the blood which resembles the lardaceous material in its chemical reactions, has never been made out even in the most marked cases of the disease. This

fact must therefore negative the supposition that it is a simple infiltration. If the new material be derived from the blood at all, it must undergo some chemical change subsequently to its deposition in the tissues. Dr. Dickinson considers that it is dealkalised fibrin, which is deposited in consequence of the loss of the alkali which it normally contains. This loss of alkali he attributes to the chronic suppuration which usually precedes the disease, pus containing large quantities of potassium and sodium salts. He consequently terms the disease "depurative infiltration."* Whatever be the exact nature of the change, it is probably due to some abnormal state of the blood; although whether the new substance found in the organs is a deposition, or an altered condition of the albumen of the tissues due to the altered blood, must for the present remain uncertain.

LARDACEOUS DEGENERATION OF THE LIVER.

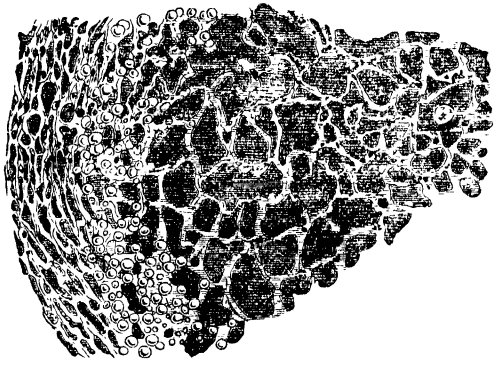
The liver is one of the most frequent seats of the lardaceous change, and here, as in other parts, it probably commences in the small nutrient blood-vessels, although the alterations are much the most marked in the hepatic cells. If a liver be examined in the earlier stages of the affection, and the iodine solution applied to thin washed sections of the organ, it will be found that the characteristic staining is limited to certain portions of the lobules—viz., to those which are situated between their external and central parts. This intermediate portion corresponds with the distribution of the hepatic artery, and the ramifications of this vessel, together with the hepatic cells situated in their vicinity, are the first to become affected. (Fig. 19.) As the change advances the whole lobule may ultimately become involved. The alterations in the hepatic cells are very characteristic. They are much enlarged, irregular in outline, their nuclei are imperceptible, and

* "Medico-Chirurgical Transactions," vol. l.

many of them are fused together into irregular-shaped masses. (See Fig. 18.)

The earliest seat of the lardaceous change thus differs from that of the fatty. In fatty infiltration it is the most external portion of the lobule in which the fat first accumulates—that which corresponds with the distribution of the portal vein. (See Fig. 8.) It differs also from that pigmentation of the hepatic cells, resulting from mechanical congestion, which takes place in the most central

FIG. 19.



Lardaceous Liver. A portion of one lobule, showing the enlargement and fusion of the hepatic cells, and the greater implication of the intermediate zone of the lobule. At the more external portion of the lobule are seen several fat cells, a certain amount of fatty infiltration being associated with the lardaceous change. *v.* Hepatic vein. × 100.

portion, around the hepatic vein. (See "Nutmeg Liver.") Thus in each hepatic lobule three zones may be distinguished:—an external one, which is the chief seat of the fatty change; a central one, which is the chief seat of the pigmentary change; and an intermediate one, which is the chief seat of the lardaceous change. These three zones, indeed, may frequently be recognised by the naked eye, the pale opaque external one contrasting strongly

with the intermediate one which is translucent, and with the darker central one. In the most advanced stages of the disease, however, both the external and central portions of the lobule may become involved, and the cut surface present an almost uniformly homogeneous appearance.

The lardaceous liver is increased in size, often very considerably so; it may be so large as almost completely to fill the abdominal cavity. The enlargement is uniform, and hence the natural configuration of the organ is but little altered. Its weight is increased, and also its specific gravity. Its edge is rounded, the surface is smooth, and the capsule appears tense and stretched. The consistence is firm and elastic. The cut surface is dry, bloodless, smooth, translucent, and waxy-looking, and of a pale reddish-grey or dirty yellow colour. If the change is very far advanced, the tissue may be perfectly homogeneous, all distinction between the individual lobules being lost. In other cases the lobules are distinctly mapped out; they are enlarged, and the external zone may be of an opaque yellowish-white colour owing to the presence of fat. This association of the fatty and lardaceous changes is exceedingly common. Lardaceous degeneration does not obstruct the portal circulation, and hence does not cause ascites. It impairs the vitality of the hepatic cells, and thus interferes with the functions of the organ.

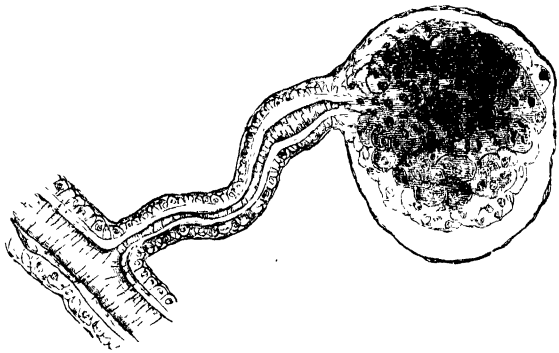
LARDACEOUS DEGENERATION OF THE KIDNEYS.

The kidneys are very liable to be involved in the lardaceous change, and here it is the smaller blood-vessels which are more especially affected. It may constitute in them the primary lesion, or it may occur subsequently to inflammatory conditions implicating the secreting and interstitial structures. As a primary change it is sometimes described as a variety of Bright's disease.

The process usually commences in the tufts of vessels which form the Malpighian bodies, the walls of which

become thickened by the new material, so that the tufts are increased in size. It then involves the small afferent arteries, and ultimately the vasa efferentia and the arteriolæ rectæ which run through the medullary portion of the organ. The changes produced in the vessels are very characteristic. Their walls are considerably thickened, and their calibre is so much diminished that the smallest ones cannot be artificially injected. This thickening of

FIG. 20.



Lardaceous Degeneration of a Malpighian Tuft and small Artery of the Kidney. Showing the thickening of the walls of the vessel, the enlargement of the cells of the circular muscular coat, and the homogeneous layer formed by the intima and longitudinal muscular fibres. × 200, reduced ⅓.

the walls of the vessels is mainly owing to alterations in their muscular coat, and especially to the cells of the circular muscular layer. These cells are much increased in size, they are more or less globular in shape, and many of them have lost their distinctive outlines. The longitudinal muscular fibres and the most internal coat of the vessel are often seen as one homogeneous, glistening, structureless layer. (Fig. 20.) After the vessels have become affected, the intertubular tissues of the cortex are involved, and in some cases the epithelium of the tubes

also undergoes the lardaceous change. In the earlier stages of the process, however—if the organ is not the seat of any other morbid change—the tubes and their lining epithelium present a perfectly natural appearance. Many of them contain pale hyaline casts, which also appear in the urine. These, however, are probably simply exudation products; although, from the reaction they occasionally exhibit, it appears that they sometimes consist of the same material as that which permeates the vessels and intertubular structures. As the change proceeds, and the new material increases in amount, the tubes become compressed, and in many places completely obstructed. If the compression is not uniform, they may dilate and form small cysts. The epithelium, which was at first normal, owing to the interference with its nutrition, ultimately atrophies and undergoes fatty changes. In some cases it appears to be the seat of a catarrhal process, and the tubes are found blocked with the epithelial products. In the later stages of the process there is almost invariably an increase in the intertubular connective tissue.

The first effect of this change is to obstruct the circulation in the cortex. The blood-vessels, diminished in calibre, allow little but the liquor sanguinis to pass through them, the passage of the blood-corpuscles being to a great extent prevented: hence the pallor of this portion of the organ. The arterial walls are so altered that fluids and albumen readily permeate them; and thus is produced the large quantity of urine, loaded with albumen, which characterises the earlier stages of this affection. As the change proceeds, and the tubes become obstructed, the urine diminishes in quantity. The excretion of urea is less interfered with than in other forms of Bright's disease, and hence symptoms due to its retention seldom occur. Tube casts are rarely numerous; they are for the most part hyaline or finely granular, though sometimes they are covered with fatty epithelium.

In the earlier stages of the affection, the cortex of the

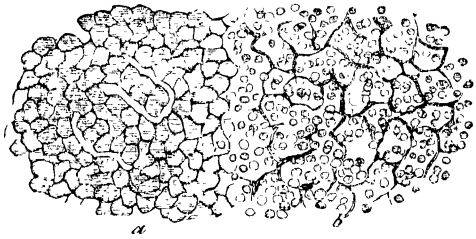
kidney is merely rather paler than natural, and perhaps somewhat firmer in consistence; but otherwise it presents no abnormal appearance. It is only upon the application of iodine to the cut surface, or to thin washed sections of the organ, that its diseased condition becomes evident. When this test is employed, the Malpighian bodies at once become apparent as minute red points scattered through the cortex. As the disease advances, the size of the organ increases; the enlargement, however, is principally confined to the cortex. The surface is smooth, and the capsule separates readily. The enlarged cortex is remarkably pale and anæmic, and has a peculiar transluceut, homogeneous, wax-like appearance. Its consistence is hard and firm. A few scattered vessels may be seen on the surface, and the bases of the pyramids sometimes exhibit an increased amount of vascularity. If iodine be poured over the cut surface, the Malpighian bodies and the arteries of the cortex become mapped out almost as clearly as in an artificial injection. The enlarged Malpighian bodies may indeed usually be seen as glistening points before the iodine is applied. Frequently, the homogeneous appearance of the cortex is interrupted by minute, opaque, yellowish-white lines and markings; these are produced by the fatty changes in the epithelium of the tubes, which so commonly occur in the later stages of the affection. Ultimately the capsule becomes more or less adherent, and slight irregular depressions make their appearance upon the surface of the organ: the latter are due to atrophic changes in some of the tubes. If, as is usually the case, the process is associated with an increase in the intertubular connective tissue, the atrophy of the organ will be more marked. (See "Interstitial Nephritis.")

LARDACEOUS DEGENERATION OF THE SPLEEN.

Lardaceous degeneration of the spleen is met with in two forms—one in which the disease is limited to the

Malpighian corpuscles—the **Sago Spleen,** and the other in which the pulp appears to be chiefly implicated. The former is much the more common condition. In it the Malpighian corpuscles undergo the lardaceous change, and become converted into translucent wax-like bodies, much like boiled sago; hence the name. The process commences in the small arteries of the corpuscle, and then the lymphatic cells, of which the corpuscle is made up, are involved; they increase in size, become more irregular in outline, many of them coalesce, and ulti-

FIG. 21.



Lardaceous Degeneration of the Spleen—"*Sago Spleen.*" A portion of one of the altered Malpighian corpuscles, *a*, with the adjacent normal splenic tissue, *b*. Showing the increase in size, and in many parts, the coalescence of the cells, of which the corpuscle is composed. × 200.

mately the whole is converted into a pale, firm, translucent, glistening mass. (Fig. 21.)

The sago spleen is more or less enlarged; its weight and density are also increased. The cut surface is smooth, dry, and studded all over with small glistening sago-like bodies, varying in size from a millet to a hemp-seed, which are stained a reddish-brown colour by the iodine solution. These may become so large as to occupy a large portion of the organ, although in earlier stages of the affection they are so minute that they can only be seen in thin sections of the tissue.

In the other variety of lardaceous spleen, the pulpy

parenchyma between the corpuscles is principally affected. This is probably merely an advanced stage of the former condition, in which the disease extends from the corpuscles to the surrounding pulp; the whole organ being ultimately involved. Under these circumstances the organ often attains a considerable size, much larger than is met with in the sago spleen. It is remarkably hard and firm, and the capsule is tense and transparent. On section it presents a dry, homogeneous, translucent, bloodless surface, of a uniform dark reddish-brown colour. Thin sections can be readily made with a knife, the organ cutting like soft wax. The corpuscles are not visible as in the former variety, being probably obscured by the surrounding pulp.

LARDACEOUS DEGENERATION OF LYMPHATIC GLANDS.

In the lymphatic glands the process much resembles that in the spleen. The small arteries in connection with the follicles of the gland are the earliest seats of the change; and from these it extends to the lymphoid cells. The follicle thus becomes ultimately converted into a small homogeneous mass.

The glands are enlarged, and on section the minute wax-like bodies can often be seen scattered through the cortex. The cut surface is smooth, pale, and translucent.

As these glands are largely concerned in the formation of the blood-corpuscles, their implication in the lardaceous change must to a large extent aid in producing the emaciation and anæmia which characterise this affection. The same is true of the spleen, which is usually simultaneously involved.

LARDACEOUS DEGENERATION OF THE ALIMENTARY CANAL.

The whole of the alimentary tract may be the seat of the lardaceous change, and here it assumes an important aspect from the deleterious influence which it exercises upon the absorbent and secreting processes, and from the consequent impairment of the general nutrition which results. The disease, however, in this situation is very apt to escape observation, as it produces but little alteration in the appearance of the parts. The mucous membrane may look somewhat pale, translucent, and œdematous, but otherwise to the naked eye nothing is discoverable. It is only upon the application of iodine to the washed mucous surfaces that the nature of the change becomes apparent. In the small intestine—which is perhaps the part most commonly affected—the effect of the application of iodine is very characteristic. A number of small reddish-brown points appear over the whole surface of the membrane; these correspond to the intestinal villi, the arteries and capillaries of which have undergone the lardaceous change. In the stomach and œsophagus the vessels are mapped out in a similar manner by the iodine solution. The change in the intestine gives rise to serous diarrhœa, this being probably due to an increased permeability of the degenerated walls of the vessels.

THE CORPORA AMYLACEA.

The corpora amylacea or "amyloid bodies," so frequently met with in the nervous system, in the prostate, and in other parts, have usually been looked upon as more or less allied to the lardaceous substance; there appears, however, with the exception of a certain similarity in their behaviour with iodine and sulphuric acid, to be no connection between them.

They are round or oval bodies, formed of a succession

of concentric layers, and are often changed to a deep blue colour by iodine, thus bearing, both in their structure and chemical properties, a strong resemblance to granules of vegetable starch. (Fig. 22.) Sometimes, however, the blue is only exhibited after the subsequent addition of sulphuric acid, and thus a resemblance is shown to the lardaceous substance. They vary in size from microscopic granules to bodies which are distinctly visible to the naked eye; sometimes being as much as one or two lines in diameter. The larger ones are usually formed by the conglomeration of the smaller granules, which are often enclosed by a common envelope.

FIG. 22.

Corpora Amylacea from the Prostate. (Virchow.)

They occur especially in conditions of atrophy or softening of the nervous system; the ependyma of the ventricles, the white substance of the brain, the choroid plexus, the optic nerve and retina, and the spinal cord being their favourite seats. The larger forms are met with most frequently in the prostate. The prostate of nearly every adult contains some of these bodies; and they may accumulate here to such an extent as to form large concretions. They are occasionally met with in the lungs, and in mucous and serous membranes.

As has been said they usually exhibit a bright blue colour upon the application of iodine alone, although in some cases not until the subsequent addition of sulphuric acid. Many of them, however, are coloured green, or even brown by these reagents. The green is due to their admixture with nitrogenous matters, which give a yellow colour with iodine, and hence the combination yields a green. The greater the amount of nitrogenous matter the more brown does the colour become.

From the laminated structure of these bodies they would appear to be formed by the gradual precipitation

of some material, layer by layer, upon the surface of pre-existing particles. The nature of the material, however, does not appear to resemble that of the substance met with in lardaceous degeneration. The two processes are so different, both in the circumstances under which they occur and in the characters and seat of the morbid products, that they cannot be looked upon as *analogous*. Lardaceous degeneration is a general change, whereas the formation of the corpora amylacea is evidently of a local nature. The latter is often preceded by those local atrophic changes associated with advanced life, and appears to consist in the deposition of some material, probably liberated in the tissues themselves, upon any free body which may exist in its vicinity.

The corpora amylacea, especially those occurring in the choroid plexus and in the lateral ventricles, are very liable to become calcified, and they then constitute one form of "brain sand," which is so often met with in these situations.

CHAPTER VII.

CALCAREOUS DEGENERATION.

Calcareous Degeneration—or, as it is more commonly called, **Calcification**—consists in the infiltration of the tissues with calcareous particles. Physiologically, an infiltration of calcareous particles takes place in the formation of bone, in which lime and magnesian salts are deposited in the fibrous or cartilaginous matrix. This physiological is precisely similar to the pathological process. It is important, however, to distinguish simple calcification from ossification. In the latter there is not only a deposition of lime salts, but an **active** change in the tissue itself—a proliferation of the cellular elements, an intimate union of the calcareous matters with the tissue, and the

formation of a true osseous structure in which the calcareous particles are not visible. Calcification, on the other hand, is a purely **passive** process: there is no increased nutritive activity of the part, no multiplication of elements, no alteration of the structure, but merely an infiltration with calcareous particles.

An infiltration and deposition of calcareous substances occurs under two opposite conditions: one—in which there is an absolute increase in the amount of these constituents in the blood, and a portion of the excess becomes deposited in the tissues; the other—in which there is no such increase, but the deposition takes place owing to some alteration in the tissue itself. That the calcareous particles are in all cases brought to the part, and are not simply those normally contained in it which have become precipitated, is shown by the fact that their quantity greatly exceeds that of healthy tissue.

An absolute increase of the saline constituents in the blood, and the deposition of the excess in the tissues, is much the less frequent form of calcification. It occurs in some forms of softening of bone, especially in extensive caries and osteomalacia. In these diseases the lime salts are removed from the bone, returned into the blood, and some of them deposited in other tissues. In such cases the calcification is usually more or less general—many organs being simultaneously involved. In osteomalacia it is not uncommon to find the kidneys, the lungs, the stomach, the intestines, and even the dura mater and liver, infiltrated to a greater or less extent with lime salts. The deposition takes place in the tissue immediately surrounding the blood-vessels, through the walls of which the calcareous matters transude;—thus, in the lungs the seat of the change is the interlobular tissue; in the stomach, the stroma between the glands; and in the kidney, the tubuli uriniferi and the intertubular tissue. Analogous to this form of calcification is the deposition of the excess of urate of soda which takes place in gout.

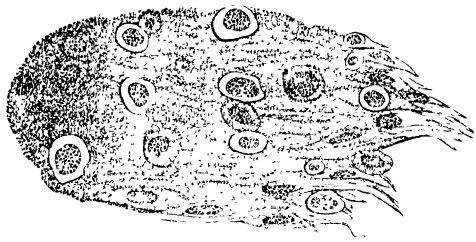
In the great majority of cases, however, calcification is

a local change, depending not upon any alteration in the composition of the blood, but upon changes in the tissues themselves, owing to which some of the saline matters which are normally held in solution in the blood are deposited in them. The alteration in the tissues *consists in* some enfeeblement of the nutritive processes, *associated* with a diminution in the amount of blood, and a retardation of its circulation. Calcification is therefore very frequent as a senile change, and is especially common in the arteries of old people. (See "Calcification of Arteries.") It also occurs under other circumstances where tissue changes are very feeble, as in thrombi, in the caseous masses so common in the lungs and lymphatic glands, in atheromatous arteries, and in non-vascular tumours. Respecting the cause of the deposition of the calcareous substances—it is probably partly due, as stated by Rindfleisch, to the stagnation of the nutritive fluids in the part, owing to which the free carbonic acid, which appears to hold the salts in solution, escapes, and they are consequently precipitated; and partly to the non-assimilation of these fluids by the enfeebled elements of the tissue.

The calcareous particles make their appearance both within the cells and in the intercellular substance; they are much more frequent, however, in the latter situation. They are seen at first as fine molecules scattered irregularly through the intercellular substance. (Fig. 23.) They are characterised, when viewed by transmitted light, by their opacity, dark black colour, and irregular outline, and also by their solubility in dilute mineral acids. They gradually increase in number until ultimately large tracts of tissue may be converted into an opaque calcareous mass, in which the cells are enclosed and can no longer be recognised. These larger masses have a sharp black irregular outline, and as the calcification becomes complete, acquire a homogeneous, glistening, semi-transparent appearance. The cells themselves are much less frequently infiltrated, being usually merely enclosed and obscured by the calcified intercellular sub-

stance. Calcareous particles may, however, make their appearance in the protoplasm, and, gradually increasing, convert the cell into a homogeneous calcareous body.

FIG. 23.



A Calcified Sarcomatous Tumour. Showing the minute calcareous particles scattered through the intercellular substance. To the left of the figure they are so abundant as to almost completely obscure the cells. × 200.

The calcareous matters consist, for the most part, of lime and magnesian salts, especially the phosphates and carbonates. If the latter are present, the addition of a little dilute hydrochloric acid is followed by the appearance of numerous minute air bubbles in the tissue, owing to the liberation of carbonic acid. In those cases in which calcification is associated with retained gland secretions, the calcareous matters will consist of the specific gland salts.

A part which has become calcified undergoes no further change; its vitality is completely destroyed, and it remains as an inert mass. In this respect calcareous differs from fatty degeneration. In the latter, subsequent changes invariably take place; the part either softening, caseating, or becoming the seat of calcification itself. It differs also in its effect upon the tissue. The structure of the affected part is not destroyed, and there is no annihilation of histological elements, such as occurs in fatty degeneration. The tissue is simply impregnated with calcareous matters, which have no other effect upon

it than to render it inert; its vitality is destroyed, but its structure—in so far as the calcification is concerned—remains unaltered. If the saline matters are dissolved out with a little dilute mineral acid, the structure of the part may be again recognised, unless, indeed—as is so often the case—it has been destroyed by any antecedent change.

Calcification must thus be looked upon in many cases as a salutary lesion, the impregnation with calcareous matters preventing subsequent changes in the part. This is especially the case when it is secondary to other forms of degeneration. It is often the most favourable termination of the large class of fatty changes, as is exemplified by the calcification of caseous products in the lungs, and of many new formations. It may, on the other hand, under certain circumstances, be attended with most deleterious consequences, as is the case when it affects the arterial system.

CALCIFICATION OF ARTERIES.

Calcification of arteries, like fatty degeneration, may be a **primary** or **secondary** affection. As a secondary change it constitutes one of the terminations of the atheromatous process, and as such is constantly met with in the aorta and its branches, and in many other situations. (See "Atheroma.")

Primary calcification is essentially a senile change, and is the result of that impairment of the nutrition of the arteries which exists in advanced life. It is associated with atrophy of the arterial tissues, and in some cases with fatty degeneration. The change is a more or less general one, and when occurring in one part is met with in others. It usually occurs in vessels of medium size, the arteries of the upper and lower extremities and of the brain being those most commonly affected. Its most common seat is the middle coat, where it commences in the muscular-fibre cells. The calcareous particles, which are deposited from the vasa vasorum, make their appear-

ance at first around and within the nucleus, and gradually increase until they fill the cell, which becomes converted into a small calcareous flake. The process may go on until the muscular coat is completely calcified, or it may be limited to isolated portions of the coat, giving rise to numerous calcareous rings and plates which are irregularly distributed throughout it. From the muscular it may extend to the external and internal coats, until ultimately the vessel becomes calcified throughout.

The vessel thus calcified loses its elasticity and contractility ; its lumen is diminished, and it is transformed into a hard, rigid, brittle tube. This condition is common in the external iliac and in the vessels of the lower extremity, where it is a frequent cause of senile gangrene. (See "Senile Gangrene.")

CHAPTER VIII.

PIGMENTARY DEGENERATION.

Pigmentary Degeneration, or Pigmentation, consists in an abnormal formation of pigment in the tissues. All true pigments are derived from the colouring matter of the blood. Physiologically, many of them are eliminated by the kidneys and liver; others are deposited in the tissues and there remain permanent. The choroid coat of the eye and the skin of the negro are well known examples of tissues in which there is this permanent accumulation of pigment. The cells in these situations appear to be endued with a special power to abstract the colouring matters from the blood, and to store them up in their interior, where they undergo certain chemical changes and become converted into pigment.

In the pathological process, also, the pigment is derived from the same source, although its presence in the tissues is rarely dependent upon any abnormal secreting powers

in their cellular elements, but is usually the result of certain changes in the circulation or in the blood-vessels, owing to which the colouring matter of the blood escapes and infiltrates the surrounding parts. This escape of hæmoglobin may be owing to rupture of the vessels themselves, or to conditions of congestion or stasis in which the blood-corpuscles and liquor sanguinis pass through their walls. In either case the hæmoglobin will permeate the tissues and ultimately be converted into pigment. Rupture of the vessels and the direct extravasation of blood, is, however, the most common antecedent of the pigmentary change. Soon after the extravasation has taken place, the hæmoglobin escapes from the red blood-corpuscles, either by exudation or by destruction of the corpuscle, and, mixed with the liquor sanguinis, infiltrates the surrounding tissues. In other cases the process takes place without any solution of continuity in the walls of the vessel. This frequently occurs in conditions of inflammatory stasis and mechanical congestion, in which the red corpuscles pass through the walls of the capillaries, and some of the hæmoglobin is also liberated from the corpuscles within the vessels, from which it transudes, dissolved in the liquor sanguinis, without rupture having taken place. In whichever of these ways the hæmoglobin is derived, it infiltrates the tissues, staining both the cells and the intercellular substance a yellowish or brownish-red colour. It is taken up, however, more readily by the cells than by the intercellular substance or by membranous or fibrous structures. In addition to this formation of pigment from dissolved hæmoglobin, the red corpuscles themselves may penetrate the adjacent cells and there become converted into pigment. Some of the corpuscles also, after their escape from the vessels, may shrivel up and become pigment granules. It is probable that in some cases these changes and the subsequent formation of pigment may take place within the vessels.

After the hæmoglobin has remained in the tissue for

some length of time, it undergoes certain changes:—It becomes darker and more or less granular, minute reddish-brown or black granules and crystals make their appearance both in the cells and in the intercellular substance, and these may gradually increase and form larger masses. This change in the hæmoglobin is a chemical one, and the substance into which it is converted is **hæmatoidin.** Hæmatoidin appears to be closely allied to the colouring matter of the bile, cholepyrrhin, which is also a derivative of hæmoglobin. It exhibits similar reactions when treated with concentrated mineral acids, displaying the same variations of green, blue, rose, and yellow colours. It is insoluble in water, alcohol, ether,

FIG. 24.

Cells containing pigment. From a melanotic sarcoma of the liver. × 350.

FIG. 25.

Hæmatoidin crystals. (Virchow.)

and in dilute mineral acids and alkalies; it is soluble in the caustic alkalies, giving a red colour. It contains more carbon than hæmoglobin; and it also contains iron.

The granules of hæmatoidin vary in size from the smallest particles to masses as large as a red blood corpuscle. (Fig. 24.) The larger ones are round, or more commonly irregular in shape, and have a sharp defined border. Their colour varies from yellow, red, and brown, to black. These variations appear to depend upon the age of the granules and the tissue in which they are formed; the older they are the blacker they become. The smaller granules are usually dull and opaque; the larger ones, however, often present a more or less glisten-

ing appearance. The crystals of hæmatoidin are opaque rhombic prisms, usually of a beautiful yellowish-red or ruby-red colour, sometimes approaching to brown or black. They may also occur as little plates and fine needles, but these are less common forms. (Fig. 25.) They are in most cases so small that considerable care is required to recognise their crystalline nature under the microscope, and they may easily be overlooked as merely irregular granular masses. In some cases, however, they attain a larger size. They are more or less transparent, and present a shining, strongly refracting surface.

Whether the hæmoglobin is converted into granular or crystalline hæmatoidin appears partly to depend upon the tissue in which it is situated, the crystals being exceedingly common in some situations, as in the brain and ovaries, whereas in others, as mucous membranes, only the granules are met with. Both the granules and crystals are characterised by their durability and by their great powers of resistance; when once formed they undergo no further change.

Those forms of pigment—both granular and crystalline—which are of an intensely black colour, have been supposed to consist of a substance which differs in chemical composition from hæmatoidin, and which has been called **melanin.** There appears, however, to be no foundation for such a distinction. Melanin is probably merely hæmatoidin which has become more or less altered by age. It is endued with greater powers of resistance, being less readily soluble in reagents than the more recently formed hæmatoidin, and it contains more carbon.

Pigmentation, although one of the most common forms of degeneration, is of comparatively little importance as a morbid process. The mere existence of pigment within and between the histological elements of the tissues, has in itself but little influence upon their vitality and functions. The atrophy and impairment of function which so frequently accompany it must rather be looked upon as

the result of those conditions upon which the formation of the pigment depends, than as in any way owing to the presence of the pigment itself.

As evidence of other antecedent conditions, pigmentation assumes a more important aspect. The pigment being derived from extravasated hæmoglobin, in whatever situations it occurs, it is usually to be looked upon as the result of some alteration in the circulation or in the blood-vessels, owing to which the escape of the colouring matter is permitted. Exceptions to this exist, however, in the case of certain pigmented new formations, in which the presence of the pigment appears to be mainly owing to the selective power of the cells; these, like those of the choroid, separating the colouring matter from the blood. It is those growths which originate in tissues normally containing pigment, as the choroid and rete mucosum, which are most frequently melanotic. (See "Melanotic Sarcoma.") In Melanæmia, again, the large quantities of pigment which exist in the blood are probably the result of a local formation—for the most part by the spleen. Lastly, in Addison's disease, the pathology of the pigmentation of the skin is at present involved in obscurity.

Pigment is often the only evidence of a former extravasation. *This is frequently the case in cerebral hæmorrhage, where the crystals of hæmatoidin may be* all that remains to indicate that rupture of the capillaries has taken place. In the ovaries, also, the slight hæmorrhage which follows the escape of the ovum at each menstrual period is marked by the formation of pigment which constitutes the "corpus luteum." In mechanical congestion and inflammation, again, the consequent pigmentation may be the principal evidence of the former existence of these conditions: this is especially seen in pigmentation of the mucous membrane of the stomach and intestines. The formation of pigment is thus, with the few exceptions above named, the result of some antecedent change in the blood-vessels or circulation; and its presence in the tissues appears to be little more than a

testimony to the existence of those processes upon which its formation depends.

FALSE PIGMENTATION.—There are certain forms of discoloration of the tissues which are not due to the presence of hæmatoidin: these must be distinguished from true pigmentation. The most important of them, and that which is most closely allied to the process already described, is the staining of the tissues with the colouring matter of the bile, which is itself a derivative of hæmoglobin, and is, as before stated, very analogous to hæmatoidin. This yellow staining may affect nearly all the tissues, constituting "jaundice;" or it may occur in the liver alone, from local obstructions to the small bile-ducts, as is often seen in cirrhosis of that organ. In these cases, however, there is merely the staining of the tissues with the colouring matter of the bile and no subsequent conversion of this pigment.

The discoloration caused by the long-continued use of the salts of silver must also be distinguished from pigmentation: the colour here is due to the deposition of the silver in the tissues. The black colour of gangrenous parts, and that sometimes produced by the effusion of large quantities of blood into the tissues, must again not be confounded with pigmentation. The discoloration in these cases is the result of the action of the sulphuretted hydrogen upon the colouring matter of the blood. The greenish-black discoloration so often seen on the surface of the liver, kidneys, and other abdominal organs after death, is in the same manner due to the intestinal gases. Lastly, the minute particles of inhaled carbon which are always met with in the lungs must be distinguished from true pigment.

PIGMENTATION OF THE LUNGS.

In no organs is pigment met with so frequently and in such large quantities as in the lungs, and here much discussion has arisen as to its nature and origin. The lungs

normally contain more or less black pigment, the amount of which gradually increases with advancing age—the lungs of infants and young children being almost free from it, whereas those of adults invariably contain it in considerable quantities.

This normal pigmentation of the lungs is principally due to the presence of carbon, and not to that of true hæmatoidin-pigment. The carbon—which is derived from the incomplete combustion of wood, coal, and other substances, and is always present in varying quantities in

FIG. 26.

Pigmentation of the Lung. From a woman, æt. sixty-five, with slight emphysema. Showing the situation of the pigment in the alveolar walls, and around the blood-vessel *v*. × 75.

the atmosphere—is inhaled, and the minute particles pass into the finest bronchial tubes. Having entered the bronchi, many of them are taken up by the mucus-corpuscles, where they may be seen as small black granules within the cells. These may readily be observed in the cells of the greyish-black sputum which is so frequently expectorated in the early morning. Much of the carbon thus inhaled is eliminated by expectoration many of the particles, however, pass into the air-vesicles,

and here their removal by this means being less readily effected, they gradually penetrate the pulmonary substance, and make their way into the alveolar walls and interlobular tissue. It is in these situations that most of the pulmonary pigment is found, and there it may be seen either within the connective-tissue cells, or lying free amongst the fibres. (Fig. 26.)

The means by which the particles of carbon penetrate the walls of the air-vesicles, and make their way into the inter-alveolar tissue, has been explained by the researches of Dr. Klein on the histology of the lungs.* Dr. Klein finds that the branched connective-tissue cells of the alveolar walls send a process, or a greater or less portion of their body, between the epithelial cells of the alveolus into the alveolar cavity. As these connective-tissue cells lie in the serous canals, which constitute the commencement of the perivascular lymphatics, it is easy to understand how these openings in the alveolar walls (pseudostomata) may become sufficiently distended to allow cells and other substances to pass through them from the alveolar cavity into the inter-alveolar tissue. When once the carbon has made its way into the interlobular tissue, some of it is taken up by the fixed cells in this situation, whilst that which is not thus detained passes on to the lymphatics, and is deposited in the bronchial lymphatic glands, where the black particles are also visible.

Closely allied to this physiological pigmentation of the lung from the inhalation of carbon, are those morbid conditions which result from the inhalation of particles of coal, stone, iron, and other substances—of which the lungs of miners, stonemasons, and grinders afford frequent examples. Here also minute particles enter the bronchi, penetrate the walls of the alveoli, and are deposited principally in the interstitial tissue. In the

* "On the Anatomy of the Lymphatic System of the Lungs," by Dr. E. Klein. *Proceedings Royal Society*, No. 149. 1874.

case of miners—in which this is most common—the particles of coal enter the lungs in such large quantities as to give to them a uniform dark black colour. In stonemasons, grinders, &c., the lungs also become deeply pigmented, although to a less extent than those of miners.

The black colour of the lungs in these cases, however, is not entirely due to the presence of the inhaled substances, but partly to that of true hæmatoidin-pigment. The inhalation of the irritating particles sets up inflammatory changes in the bronchi and pulmonary tissue, causing chronic bronchitis, chronic catarrhal pneumonia, and a large increase in the fibrous tissue of the lungs, which thus ultimately become consolidated, excavated, tough, and fibrous ("Colliers" and "Knife-grinders' Phthisis," &c.). Owing to these structural changes there is a considerable escape of colouring matter, either from rupture of the capillaries or transudation of serum, and hence a large formation of true pigment; and to this true pigment much of the dark colour of these lungs must undoubtedly be ascribed. The lungs of stonemasons and grinders are, like those of miners, deeply pigmented, although to a less degree; but the black colour in the former cases cannot be entirely accounted for on the supposition that it is due to the presence of inhaled particles.

Pigmentation of the lungs from the presence of hæmatoidin occurs as the result of many other morbid conditions, many diseases of these organs being attended by the formation of pigment. In chronic phthisis, pigmentation occurs, partly as the result of the inflammatory process, and partly from the obstruction of the vessels caused by the new growth:—lines of pigment are constantly seen surrounding the nodules of consolidation. In acute croupous pneumonia, the blood which is extravasated into the air-vesicles, and which in the early stages gives to the expectoration a rusty or prune-juice colour, subsequently becomes converted into pigment, and the sputum becomes of a greyish-black; the pigment granules

being visible in the newly-formed cells. The cells met with in the sputum of bronchitis also contain granules of pigment (Fig. 27); and pigmentation plays an important

FIG. 27

Cells from the Sputum of Acute Bronchitis. Showing the minute granules of pigment within the cells. Some of the cells also contain a few fatty molecules. × 400.

part in the condition of the lungs known as brown induration. (See "Brown Induration of the Lungs.")

Pigment in the lung usually occurs as black irregular granules; it is rarely met with in a crystalline form. In all cases in which it is found in any quantity in the lung it is also found in the bronchial glands. It is taken up by the lymphatics and, like the inhaled carbon, it becomes arrested in its passage through these glands, where it remains permanently.

CHAPTER IX.

TISSUE-CHANGES IN PYREXIA.

IT is proposed in the present chapter to allude very briefly to those alterations in the tissues which are met with in certain pyrexial diseases, to which have been applied the terms "parenchymatous" or "granular degeneration," "albuminous infiltration," "acute," or "cloudy swelling."

It is well known that in most diseases which are accompanied by a considerable elevation of the bodily temperature, and especially in those in which the blood has undergone marked changes, the organs and tissues are found much altered after death. The diseases in which such alterations are most frequently met with are pyæmia, erysipelas, typhus, typhoid, and other acute specific fevers, and acute rheumatism. They also occur in other diseases which are attended by considerable pyrexia, but they are most marked in the specific fevers, and appear to depend more upon the alteration of the blood in these fevers than upon the amount of elevation of the bodily temperature. The organs in which the alterations principally occur are the liver, the kidneys, the heart and muscles, and the lungs. Sometimes the changes are much more advanced in some organs than others, owing probably to differences in the local circulation.

The physical characters of the altered organs vary. It may, however, be stated generally that the organs are

FIG. 28.

Liver from a case of Acute Rheumatism with high Temperature. Showing the swollen and granular condition of the liver-cells. In many of the cells the nucleus is so much obscured as to be almost indistinguishable. × 200.

more or less swollen and opaque, somewhat diminished in consistence, and abnormally friable. Their vascularity is

usually diminished, but in some cases slightly increased. When examined microscopically, the cellular elements are found to be increased in size, and their protoplasm is markedly granular, so that the nucleus is often so much obscured as to be indistinguishable. (Fig. 28.) The granular condition of the protoplasm appears in most cases to be due to albuminous particles, inasmuch as it disappears upon the addition of dilute acetic acid. In other cases, however, in which the change is apparently more advanced, many of the granules are larger, insoluble in acetic acid, but soluble in ether, and obviously fatty.

The Liver.—Here the change is usually met with in its most marked degree. The organ is slightly enlarged, abnormally soft and friable, and the cut surface has a dull opaque look, being paler than natural. The liver cells are swollen and granular, and in many cases contain fatty particles. (See Fig. 28.)

The Kidneys.—In the kidneys the change affects especially the cortex. This is swollen, opaque, and friable. The Malpighian bodies and the pyramids are usually abnormally vascular, and thus contrast with the pale cortex. The epithelium in the tubes of the cortex presents the appearances above described. These are precisely similar to those met with in the earlier stages of tubal nephritis.

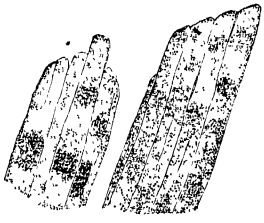
The Heart.—The alteration produced in the heart consists in slight opacity, pallor, and diminution in the consistence of the muscular tissue. Under the microscope the muscular fibres are seen to have lost their distinct striation and to be finely granular. (Fig. 29.) Such a condition must materially interfere with the contractile power of the organ. A similar change is met with less frequently in other muscles.

The Lungs.—The change in the lungs has been described by Buhl as consisting in swelling of the alveolar epithelium. The epithelial elements are markedly granular from the presence of albuminous and fatty particles, and they become loosened from the alveolar

walls. The change affects, more or less, the whole of both lungs. The organs are enlarged, œdematous, and abnormally friable.*

This change occurs not only in pyrexia, but also in the earlier stages of the process of inflammation. Here also a swollen and granular condition of the protoplasm is met with, especially in epithelial and endothelial elements. It is to this that Virchow gave the name of "cloudy swelling." (See chapter on "Inflammation.")

FIG. 29.



Muscular Tissue of the Heart, from a case of severe Typhoid Fever. Showing the granular condition of the fibres and the loss of their striation. × 400.

Respecting the nature of the change—nothing is certainly known. Dr. Wickham Legg produced it artificially in animals by submitting them to a high temperature, and he, in common with some other pathologists, is inclined to look upon it simply as a result of the high temperature. The probability that it is due rather to specific alterations of the blood has been already alluded to. An exact knowledge of its pathology, however, must await further experimental investigation. In the meantime, when it is borne in mind that the conditions in which it occurs are attended by alterations in the blood and in the nutritive processes, and that in advanced degrees of the change it is accompanied by more or less

* Buhl, "Lungenentzündung, Tuberkulose, und Schwindsucht."

fatty metamorphosis, it may be regarded as probable that its occurrence will be found to be due partly to interference with the normal processes of tissue-oxidation, and partly to increased transformation of the protoplasm of the cells. (See "General Pathology of Fatty Degeneration.")

Whatever be the nature of the change, there can be no doubt that it must very materially interfere with function, and that its occurrence in the course of acute disease, especially when affecting the heart, must constitute a most important source of danger. Although it may lead to more or less fatty degeneration, it tends, if death does not supervene, to terminate in perfect health.

CHAPTER X.

NUTRITION INCREASED.

THREE conditions must now be considered — **Hypertrophy, Regeneration,** and **Tumour-formation,** which have this in common—that in each the nutritive exchange of certain cells is so disturbed that formation exceeds waste and growth results, just as in the physiological state. Pathological growth occurs in obedience to the same laws as physiological. In hypertrophy and regeneration the structure and function of the mother-tissue are retained, and no line can be drawn between pathological and physiological tissue-formation; but in tumours the disturbance results in the formation of a mass of new tissue, which fulfils no physiological purpose, which is always a morphological, and is frequently a structural, variation from the type of the part.

Normal growth depends upon—1. The inherited tendency of the cells to grow, 2. The supply of food, and 3. The amount of waste. Pathological new-growth will be due to abnormality of one or more of these factors.

HYPERTROPHY.

HYPERTROPHY means increase in size due to enlargement or multiplication of the normal constituent elements of a part or tissue, all being affected proportionately; so that external form and minute structure are alike preserved—*e.g.*, hypertrophied heart from valve disease, or kidney after loss of its fellow. This is **true** hypertrophy, and is accompanied by increased functional power. The terms **false** or **pseudo-**hypertrophy indicate that the enlargement of an organ or part is due to overgrowth of one set of elements, often at the expense of another. It is the connective tissue which generally becomes excessive, whilst the higher tissues atrophy—*e.g.*, pseudo-hypertrophy of muscle. In these cases functional power is diminished. Both true and false hypertrophy may be extensive, involving one or more limbs; the latter, when localised, gives rise to the "hyperplastic tumours" Hypertrophy is said to be **simple** when due to increase in **size** of the elements of a part; **numerical,** when to increase in their **number.** The latter is also called **hyperplasia.** These two forms are comparable to simple and numerical atrophy. In all hypertrophies hyperplasia is constant, and may be the sole cause of enlargement; but simple enlargement of cells may occur in each tissue, and is frequent in muscle and glands. In the great example of physiological hypertrophy—the gravid uterus—it is very marked, some fibres reaching 7–11 times their normal size.

The mode of causation of hypertrophy is in many cases unknown. Often we cannot say whether a given case is due to excessive vital energy of the cells of the part, to the setting aside for its embryonic rudiment of too large a number of cells, to diminution of the resistance to growth, to an ampler food-supply, or to diminished waste. The clearest cases are those in which there is obviously an **increased supply of food.** For hypertrophy to occur, hyperæmia must be prolonged or frequently

repeated; the cells of the part must possess ability to grow, for apparently no hyperæmia would prevent a thymus from atrophying, or cause hyperplasia of adult ganglion cells; and, finally, action is necessary to active assimilation in the working tissues of the body—muscle and gland (see p. 8).

When muscle contracts frequently against an increased load, it hypertrophies—as is seen in training—unless the load is *too* heavy, when atrophy results. Frequent contraction alone is insufficient, as is shown by hands used actively but not forcibly, by hearts after years of palpitation, by bladders after the frequent micturition of pyelitis. But insert an obstruction in the circulation, or in the urinary passages, which the heart or bladder can overcome, and hypertrophy begins. Examples of these **compensatory** hypertrophies are afforded by the heart in early stages of valve disease, the bladder in stricture of the urethra, the intestine just above a permanent stricture, a vein in aneurismal varix, or any vessel through which an abnormal quantity of blood is forced.

When an organ is removed, or prevented from functionating, other organs which take on its work hypertrophy, receiving the blood which should have supplied the diseased organ as well as their own. This is best seen in the kidney; rarely in the testis and lung. Removal of one submaxillary would not cause hypertrophy of other salivary glands; this would occur only from more frequent stimulation of their secretory nerves, which probably produces the large submaxillary glands seen in epithelioma of the tongue. But the kidneys are under nerve-control to a much less extent; they seem to be excited to secrete by the presence in the blood of material suitable for their secretion, and hypertrophy naturally results from continued greatly increased supply of blood containing excess of urea, &c. Enlargement of lymphatic glands has been noted after removal of the spleen. Increased weight thrown on a bone causes thickening of it—*e.g.*, of the fibula in ununited fracture of the tibia.

Repeated hyperæmia from slight injuries causes the thickened epithelium on the labourer's hand, and a corn arises similarly. Increased blood-supply to a limb may cause lengthening of a bone, of which one epiphysis remains ununited, as has been seen in large ulcers, caries, necrosis &c. The soft parts increase secondarily. The hypertrophied spleen of intermittent fever, and the thyroid in endemic goître (Klebs), are due to active hyperæmia, perhaps excited by the presence of organisms. Exophthalmic goître has been attributed to vaso-motor paralysis from disease of the ganglia, but it is doubtful if it would result from such a lesion (p. 12).

Diminished waste is, apparently, not a common cause of hypertrophy. The best example is that of the sub-involuted uterus, the bulk of which is made up of hypertrophied muscle, and connective tissue with thick-walled vessels. Hair and nails uncut, and unopposed teeth grow till their vessels supply only nutriment enough to maintain them in their finally attained condition. The sclerosis of bone produced by small doses of phosphorus, the increase in size and strength of animals treated with small doses of arsenic, and the invigorating effect of this drug upon Styrian mountaineers, may perhaps be explained by diminished waste.

There remain certain cases in which the etiology is even more doubtful than in the above. Firstly the cases of **true giant-growth**—increase in length, rather than in breadth, being implied; hypertrophy of the whole body (giants); of half the body (rare); of whole limbs or of parts of them, as fingers and toes. Such parts are, on dissection, normal except in size. Secondly, cases of **false giant-growth** in which the connective tissue alone is increased, the part being often misshapen: lymphatics are often dilated, even to cysts, and the blood-vessels may be nævoid. Examples are met with especially in the lip (makro-cheilia), tongue (makro-glossia), and lower extremity. In some of the above, which are congenital or appear soon after birth,

there may be **excessive vital energy** or **too large a number of the cells** forming the rudiment of the part or tissue.

Nothing is known of the causation of senile hypertrophy of the prostate; nor of the enormous, but rare, enlargement of the female breast which occurs at puberty.

CHAPTER XI.

TUMOURS.

THE first notion which the name tumour conveys is that of swelling; but swelling may result from various pathological processes, and it is consequently necessary to exclude such swellings as do not conform to the idea which rises in the pathologist's mind when a swelling is described as a tumour. The features of this idea are—a formation of new tissue which is abnormal to the part; which disturbs its form, and differs from it more or less markedly in minute structure; which performs no physiological function; and which has not arisen from the causes, or with the course, of inflammation.

That tumours are formations of new tissue necessitates the rejection of all swellings due solely to retention of secretions (retention-cysts), or to extravasation of blood (hæmatoma); true hypertrophies must be rejected because—though they cause an increase in size—the shape, structure, and function are preserved. Finally, all inflammatory swellings, tumour-like products of infective inflammations (gummata, tubercle, farcy-buds, &c.), condylomata, localised œdemas and effusions —such as hydrocele—must be eliminated.

The definition of a tumour, as an **atypical new-formation** would separate the class from retention- and extravasation-cysts, and from true hypertrophies; but

many an inflammatory new-formation, as callus, or condyloma, is atypical enough both in form and structure. Moreover, there is a whole group of tumours (sarcomata) which it is impossible to distinguish anatomically from the results of inflammation. It is therefore necessary to include in a definition of tumours something which shall draw the line between them and inflammatory products; this will be that their causes, modes of origin, and often courses, are different. But as scarcely anything is certainly known of the causes of tumours, it is impossible to frame a complete, positive, definition of a tumour, which shall not be disputed by many.

DEVELOPMENT. — A tumour consists of cells, formed by multiplication of pre-existing cells, and, here as elsewhere in Nature, the characters of the parent are handed down to the offspring. In other words, a tumour belongs histologically always to the same class of tissues as the cells from which it springs (see p. 15).

In development and structure, the tumours resemble the normal tissues—every pathological growth has its physiological prototype. The resemblance, however, is by no means complete, for, as indicated in the definition, they are always more or less **atypical** in their structure. As a rule, the difference between the normal and abnormal tissue is such that with the naked eye one can tell roughly where the one begins and the other ends.

The elements from which tumours most frequently originate are those belonging to the **common connective tissue,** and to the blood-vessels and lymphatic system with which it is so intimately associated. By common connective tissue is meant that tissue which in all parts surrounds the blood-vessels, and is so universally distributed throughout the entire organism. This must be carefully distinguished from the special varieties of connective tissue—tendon, cartilage, bone, &c. In this common connective tissue we distinguish two kinds

of cells—the stable cells (connective-tissue corpuscles), and the mobile cells, which are probably wandering white blood-corpuscles. These cells are in intimate relation with the endothelium of the lymphatics, the latter vessels commencing as spaces which are universally distributed in the tissue. Further—both the endothelium of the lymphatics and that of the blood-vessels closely resemble in their physiological functions the fixed cells of the connective tissue.

In the process of development of tumours from connective tissue, the parts played by the two kinds of cells respectively cannot in our present state of knowledge be certainly stated. The first result of their activity, however, is to produce a new tissue, composed of small roundish cells, from $\frac{1}{1800}$ to $\frac{1}{2500}$ of an inch in diameter, enclosing a large ill-defined nucleus. These possess no limiting membrane, but are simply little masses of amœboid protoplasm, lying in a scanty, semi-fluid, and faintly granular intercellular material. This tissue is precisely similar to embryonic tissue. It would be impossible to determine in this early stage of the growth what it will ultimately become—whether a fibroma, a sarcoma, or an enchondroma, &c. According to the hypothesis of Cohnheim (see Etiology), the embryonic tissue is not derived from a proliferation of the elements of the mature connective tissue, but from embryonic cells which were not utilised during the period of physiological development.

The second stage of the process consists in the development of this embryonic ("indifferent") tissue into the tissue of the permanent growth, and this subsequent development closely resembles that of the immature connective tissue of the embryo. As from the immature connective tissue of the embryo are developed various connective-tissue substances — mucous tissue, fibrous tissue, cartilage, bone, &c.—so may this embryonic connective tissue, which constitutes the earliest stage of so many of the pathological new formations, become deve-

loped into various tissues, each of which resembles one of the varieties of physiological connective tissue. The embryonic tissue may undergo no higher development, the cells remaining round or oval, and the ground substance homogeneous; or the nuclei of many cells may multiply without division of the cells, forming giant-cells; or most of the cells may lengthen out into spindles, and perhaps here and there fibrillation, with disappearance of some cells, may occur. We thus get the round or oval-celled, myeloid, and spindle-celled sarcoma; also the fibro-sarcoma. General fibrillation with disappearance of most of the cells, mucous degeneration, chondrification or ossification of the stroma may occur; forming fibroma, myxoma, chondroma, osteoma; or fat may form in the cells—lipoma. A combination of two or more kinds of structure may be met with in the same tumour—as a combination of sarcoma and lipoma, of enchondroma and myxoma, and so on. What determines the ultimate development of the young cells, why they produce such various forms of growths, is as far from our knowledge as what determines the ultimate destination of the cells in the embryo.

Next to connective tissue, **epithelium**—surface and glandular—is the tissue from which tumours most frequently originate; and as from connective tissue are produced growths of the connective-tissue type, so growths originating from the epithelia preserve the epithelial type. *A priori*, it would be entirely contrary to evolution for them to do otherwise; and the great majority of observers state, as the result of their observations, that epithelium never arises but from epithelium. It is, nevertheless, believed by some that an epithelium-cell may by mere contact so influence a connective-tissue cell that it becomes epithelial, or *vice versâ*. This influence of one cell upon another is called "spermatic" (Creighton). The point has been carefully investigated by Ziegler with a negative result.

From the remaining tissues, **muscle** and **nerve**, the

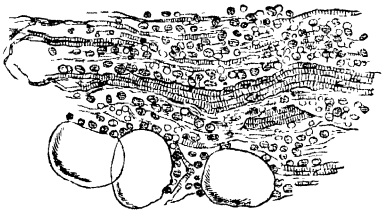
development of tumours is comparatively rare; and in the highest adult nerve-tissue it is doubtful if formative processes ever occur.

According to the similarity or difference which subsists between the new growth and the tissue from which it grows, tumours are divisible into two classes—**homologous** and **heterologous**. When the tumour resembles in its structure and development the tissue from which it *originates*, it is said to be homologous; when it differs, it is said to be heterologous. A cartilaginous tumour, for example, growing from cartilage, is homologous, but growing from any other tissue, as from the parotid gland, it is heterologous. This distinction is probably superficial—not real. If it be correct that tissue-types "breed true," the only even apparent heterology, which we know to occur, is the development of the different connective tissues from the same embryonic tissue. In the example given, cartilage does not arise from the essential epithelial cells of the parotid, but from the supporting connective tissue, or from an aberrant bit of cartilage from the rudiment of the jaw (p. 130). Heterology, however, is not limited to the production of a tissue which is dissimilar to that from which it originates; a tumour is said to be heterologous also when it differs from the tissue in which it is *situated*, and this may occur without its being the direct product of the latter. It is heterology in this sense that is so characteristic of malignant growths. Cancers, for example, become heterologous owing to the growth and extension of the epithelium beyond its normal limits (see "Epithelioma," Fig. 64); and the same form of heterology obtains in the case of all growths originating from elements which have migrated or been carried from their original habitat, and have developed into a tissue differing from that in which they are situated.

RELATION OF THE TUMOUR TO THE SURROUNDING TISSUES.—The relation of the tumour to the surrounding structures varies. In one case the tumour is circumscribed, merely displacing the surround-

ing parts, stretching and irritating their connective tissue; and this often forms a fibrous capsule around it, by which it is completely isolated. The lipomata, fibromata, and enchondromata are usually thus encapsuled. In other cases the growth invades the adjacent structures. (Fig. 30.) There is then no line of demarcation between the tumour and the surrounding parts; and although to the naked eye there may seem to be one, the microscope will show that the apparently healthy tissues are infiltrated with a small round-celled growth, into which the specific tumour-cells are advancing. The former is probably the result of tissue-irritation set up by the latter.

FIG. 30.



Scirrhus of the Mamma.—A thin section from the most external portion of the tumour. Showing the invasion by small-celled infiltration of the muscular fibres and adipose tissue in the neighbourhood of the gland. × 200.

RETROGRESSIVE CHANGES.—A tumour never actually disappears, and it thus differs from an inflammatory growth—for example, from a syphilitic gumma. It may remain stationary, or grow slowly or rapidly, and sooner or later it usually becomes the seat of retrogressive changes. The time at which these commence varies. As a rule, the permanence and durability of a tumour bear an inverse relation to the rapidity of its growth, and to the inferiority of its organisation. The more rapid the growth, and the more lowly organised the tissue formed, the less its durability and the sooner do retrogressive changes occur. The carcinomata and sarcomata,

for example, which develop rapidly, and consist for the most part of cells, quickly degenerate; their elements are unstable and soon perish. Osseous tumours, on the other hand, which develop more slowly, and consist of a more highly organised tissue, have a much greater stability, and are but little liable to retrogressive metamorphosis.

The retrogressive changes are similar to those met with in the physiological tissues. Deficient supply of blood is followed by fatty degeneration and its various terminations—softening, caseation, and calcification. Pigmentary, colloid, and mucoid degeneration also may occur. Tumours may become the seats also of inflammation, ulceration, necrosis, and hæmorrhage.

The nutrition of tumours is not regulated like that of normal tissues. When the body is getting thin, a fatty tumour wastes little or not at all; and malignant growths often grow luxuriantly when their victims are greatly emaciated.

CLINICAL COURSE.—Tumours are divided clinically into two great groups, the **simple** and **malignant.** A **simple tumour** is one which, as a rule, grows slowly and steadily, or, having attained a certain size, remains stationary. It consists of tissue approximating closely in structure to some normal adult tissue, and is generally surrounded by a distinct capsule out of which it can be completely shelled—for there is no infiltration of surrounding parts. After such removal it does not recur locally, and secondary growths in glands or more distant parts do not result from it. It interferes with health only mechanically, unless some accident—as inflammation—occur in it. Tumours of the adult connective-tissue type generally pursue this course, and may reach a huge size.

A **malignant growth,** on the other hand, generally grows rapidly and tends to enlarge continuously; consists of tissue which is markedly atypical; is, as a rule, surrounded by no capsule, but progressively infiltrates the surrounding tissues; after apparently complete removal recurs, and whether removed or not, secondary growths

are common in the nearest lymphatic glands, or in distant parts, or in both. Though the patient is often in excellent health at the appearance of the tumour, he sooner or later wastes, loses strength rapidly, and becomes very anæmic—**cachexia** is produced. This is due to many causes—*e.g.*, to removal from normal tissues of nutriment required for the active growth of the tumour-cells; perhaps to the metabolism of the latter, pouring abnormal excreta into the blood; to pain and anxiety; often to profuse discharge and septic absorption consequent upon ulceration; occasionally to actual interference with the ingestion and absorption of food. The more rapidly and the more completely a tumour produces these results, the greater its malignancy. Even growths of the same class vary much in these respects, and different classes do so still more. Though in a high degree characteristic of cancers, the purely clinical term "*malignant*" must be distinguished from the pathological term "*cancerous*," which implies a specific structure in the growth it refers to. Sarcomata are often quite as malignant as cancers.

Recurrence and Generalisation.—A tumour may recur *locally* after removal; and after or before removal, growths similar to the primary tumour may form in the nearest **lymphatic glands,** or in more **distant tissues or organs.** In the highest degrees of malignancy, all these occur. Each of these must be considered separately.

Reproduction of the Tumour in Adjacent Structures.—This recurrence *in loco* after removal is usually the earliest, and is the slightest evidence of malignancy. It is due to some of the tumour-cells having been left behind, and is therefore much more likely to occur in those growths which infiltrate the surrounding tissues, and really extend beyond their *apparent* limits, than in those which do not. The cells left behind continue to grow and recurrence occurs. Cells may be carried to some little distance from the primary growth by lymph- or blood-currents, and becoming impacted, form secondary nodules around the original tumour. In some tumours

local recurrence occurs many times, and often kills the patient without affection of glands or generalisation (see Small Spindle-celled Sarcoma, p. 158.)

Reproduction of the Tumour in the nearest Lymphatic Glands.—This is owing to the entry into and transmission by the lymph-stream of cells from the malignant growth, which become arrested in the nearest lymphatic glands, and there develop into secondary tumours. These are in all cases of the same nature as the primary tumour. When the lymphatic glands have themselves developed into secondary growths, they in their turn constitute new centres of infection, and may thus infect more distant glands or the immediately adjacent tissues. When the lymph-sinuses of a gland are so blocked by new-growth that lymph cannot pass, a regurgitant flow is the natural result, and the lymph, bearing tumour-cells, has to pass through abnormal vessels and glands. In this way we can account for affection, say, of the abdominal glands by tumour of the lung, and for the numerous nodules in the skin which sometimes occur widely all round atrophic scirrhus of the mamma. A distant lymphatic gland may be infected by embolism of its artery. The tendency to reproduction in the lymphatic glands varies very much in the different varieties of malignant growths, being, for example, very marked in the carcinomata, whereas in the sarcomata it is less frequent. The reasons for these differences will be seen in the subsequent chapters (pp. 156, 189).

Reproduction of the Tumour in Distant Tissues.—This is usually the terminal process in the history of malignant growths. The reproduction of the malignant growth in distant tissues is, in the great majority of cases, owing to the entry of some of its elements into the blood-stream. The secondary tumours are therefore the result of embolism of tumour-cells; and the points at which the cell-masses may be arrested are stated in the chapter on Embolism (p. 243). As in the lymphatic glands, they are in all cases of the same nature as the

primary one, although they are often softer, more vascular, more active in growth, and may be larger. They may constitute secondary centres of infection, and in the same way cause tertiary growths in parts beyond.

Although the general dissemination of a malignant growth is thus in most cases owing to the transmission of its elements by the blood-stream, this is not the only way in which it may be brought about. Exceptional cases have been described in which the elements of a tumour have been distributed and have caused secondary growths in other ways, as by passing down the trachea, travelling between the layers of the peritoneum, or from the kidneys down the ureters to the bladder, &c.

Lastly, it must be borne in mind that growths may be secondary to each other only *in time;* being entirely independent of each other, and originating from different primary foci.

We have spoken of generalisation and lymphatic infection as certainly due to carriage of tumour-cells from the primary growth. The similarity in structure and the time-relation of primary and secondary growths, their demonstrable connection by vascular channels, and the fact that the secondary growths often occur in tissues in which primary tumours, of their structure, never occur, prove the origin of the secondary from the primary tumour. Some authorities think that carriage of the juice and not of the cells of the primary tumour is the cause of the secondary nodules. But the localised action, the distribution of secondary growths in the next capillary area, and the possibility of explaining exceptions to this rule; the occasional finding of tumour-cells in the blood, and more often impacted in vessels as emboli; the frequent demonstration of tumour growing into veins and lymphatics, both makroscopic and mikroscopic, so that cells may easily be swept off by, or migrate into, the stream; and the fact that secondary growths have never been found in cartilage or cornea which are permeable to fluids, show that the cells rather than juice are the cause

of secondary growths. Two views are held as to how they produce this effect:—

1st. It is said that the cells impacted at a certain spot so influence the vessel-wall and surrounding tissues that their cells multiply and produce a structure like that of the infecting particle. The objection has already been stated to this spermatic influence, which would require us to believe that liver-cells, for example, may by their multiplication produce, not only epithelial cells like those of scirrhus, columnar or squamous epithelioma, but connective-tissue cells of all kinds.

2nd. The cells of the secondary nodule are believed to be the products of the multiplication of the cells of the tumour-embolus. The question thus arises—Can a bit of tumour, thus cut off from its base, grow? Artificial embolism of portions of fresh periosteum has been produced by Cohnheim and Maas, with the result that they grew and produced cartilage and then bone; but after the fifth week all trace of them had disappeared. In fact, they went through the same course as do pieces of normal tissue or of tumour which are placed in the subcutaneous tissue. We see, therefore, that they can grow; but something in the healthy tissues prevents their attaining any size.

This leads to a consideration of the **causes of malignancy.** Why do some tumours invade adjacent tissues and generalise, whilst others do not, even though they grow as rapidly or more so than those which do? Hitherto difference in structure has been held to explain the matter. The more purely cellular the tumour, the richer it is in blood-vessels, and the less developed their coats, the more rapid its spread, and the earlier and more certain its generalisation.

But occasionally we find that a tumour which has run a simple course, and which does not recur after removal, has a structure necessitating its being placed among the sarcomata. Epulides, central sarcomata of bones, some sarcomata of the ovary and fasciæ may grow to a large size without invading other tissues or generalising. On

the other hand, examples of the generalisation of many simple tumours have been frequently recorded—*e.g.*, chondroma, myxo-lipoma, even fibroma; also adenomata of the ovary and thyroid. It is true that connective-tissue growths do generally contain a preponderance of round cells before they generalise; but in some cases the structure of the secondary growths is that of the primary, and is such as is usually seen in specimens which show no malignancy. Cohnheim thinks, therefore, that the essential factor in "malignancy" is not a certain structure on the part of the tumour; but rather some change in the surrounding tissues which renders them unable to resist invasion. For, from the way in which physiological tissues lie side by side, never invading each other's precincts, though one or both may be growing actively, it is evident that each tissue possesses a power which opposes infiltration by any other tissue; this power Cohnheim calls "physiological resistance." Its existence is further shown by the experiments of Cohnheim and Maas alluded to above; which prove that bits of malignant growths or normal tissues transplanted into the tissues of a normal animal, may become vascularised and grow; but that they will shortly after disappear—the healthy tissues get the upper hand. To permit the infiltration of one tissue by the elements of another, the physiological resistance of the former must be reduced. This may be effected by (1) **Inflammation**, and therefore by injury: in chronic inflammation of epithelium-covered membranes (cirrhosis of liver, interstitial pneumonia, &c.), masses of epithelium are found in the infiltrated connective tissue (Friedländer). (2) **Age**: Thiersch showed that connective tissues atrophy after mid-life from diminished vital activity; probably diminished physiological resistance accompanies this, and thus the more active surface-epithelium is enabled to invade the sub-lying cutis. This he regarded as essential to the growth of an epithelioma. (3) **Heredity**: hereditary weakness on the part of the tissue surrounding a tumour-

germ must be assumed in young people in whom neither injury nor age can be regarded as a cause of diminished physiological resistance. But even if no tumour can infiltrate in the absence of this change in the adjacent tissues, the structure of the growth probably has a marked influence upon its malignancy. Tumours which have great power of growth, whose cells are loosely held together, whose blood-vessels are numerous and thin-walled, and whose cells actually lie in lymph-spaces, must generalise more readily, when this is possible, than tumours in which opposite conditions obtain.

ETIOLOGY.—Nothing is really known on this point. We have to account for the presence in some tissue of cells which have an *ability to grow* more or less in excess of that possessed by the normal cells of that tissue. Increased *food-supply* will of course be required, but this is of secondary importance; as also are the surrounding physical conditions, which may be favourable or unfavourable.

At first, all tumours appear to be local, and **local causes** have consequently been sought. A causal relation seems in some cases to exist between **injury or irritation** and the formation of a tumour. But we know that the effects of these influences on normal tissues are inflammation and hyperplasia, and that they produce these effects even in those who are the subjects of tumours. Further, a history of injury cannot be obtained in 15 per cent. of the cases; and the injuries followed by tumours must constitute a very small proportion of the total number of injuries. Still, it is probable that injury, by producing hyperæmia and inflammation, may bring extra food to cells ready to grow, and may diminish the physiological resistance of the tissues round them. Irritation certainly seems to have a powerful effect in certain epitheliomata; as of the scrotum in sweeps, of old scars, and in rodent ulcers; but for the vast majority of cases no local cause can be found.

The cachexia produced by malignant growths, their

very frequent recurrence, their multiplicity, and their hereditariness—all pointing to a deep affection of the whole organism, as it was thought—gave rise to the belief that they were of **constitutional** origin. This is a bad term, for it may mean "*general*," and refer to the constitution of the whole organism; or it may refer to the constitution of certain cells, and have a *local* significance. We shall therefore use the word *general*. Now, we already know how to explain cachexia, local recurrence, and multiplicity as results of a growth of the tumour, which was produced by multiplication of a few abnormal cells—*i.e.*, by a local abnormality. There is therefore no need on these grounds to consider that the physiological processes of all the cells of the organism are abnormal and tend to produce cancer; or that removal of the primary growth would be useless, because continuance of the general abnormality would reproduce the disease elsewhere. Nor does heredity lead to this conclusion; for the whole of normal development is nothing but the transmission of local peculiarities; and moreover heredity is at least as marked in multiple simple growths—fibromata, warts, lipomata, osteomata—as it is in cancers. It is probable that *all* tumours are at first *local*, and that certain of them become malignant, as above explained; also that any inherited peculiarity, which results in abnormal growth at a certain time, affects only a few cells, or it may be many foci of cells in one tissue, and not the organism at large. It is obvious, however, that neither the constitutional nor the local view makes any pretence at explaining —how the abnormal ability to grow is acquired by the cells which give origin to the tumour. Cohnheim has advanced a hypothesis, which, if true, certainly goes a step closer. It may be called the hypothesis of

Embryonic Remains.

Thinking over the hypertrophies, the excessive formations (supernumerary digits and more marked examples of monster by excess), the teratomata and other congenital tumours, all of which are admitted to be due to an

embryonic cause, many of which are hereditary, and some of which (*see* Hypertrophy) do not appear for some years after birth, it occurred to Cohnheim that all tumours might be due to developmental faults. He supposes that more cells than are needed for a part are produced; the surplus remain in an embryonic state in one spot or scattered over a whole tissue. The causes of this error, and the reason why the cells do not develop like their *confrères* and simply enlarge the part, are not known. We know little of such collections of "resting" embryonic cells, perhaps because of their small size and resemblance to leucocytes. Small nævoid spots may enlarge greatly after birth; congenital moles, which have the structure of alveolar sarcomata, may later on become malignant, and islets of cartilage from which tumours may start have been shown by Virchow to occur in the shafts of long bones. Perhaps these may be regarded as embryonic remains.

Assuming that such embryonic foci may remain among adult tissues, Cohnheim found that his view accorded well with facts observed. There would be no difficulty about the reversion of adult cells to the embryonic type; they would start with their full developmental force. Reasons for believing in the undeveloped nature of the rudiment are—that power of growth is at its greatest in the cells of the embryo, as is shown by the fact that embryonic cartilage, transplanted to the anterior chamber of the eye, grows into a regular chondroma (Leopold), whilst adult cartilage is absorbed; that many tumours are obviously distinct from the part in which they lie—*e.g.*, adenoma of mamma is encapsuled, and its ducts do not open into those of the normal gland; and that tumours are not subject to that regulating mechanism which renders the metabolism of each tissue subservient to the good of the tissues generally.

A large proportion of all tumours occur at points at which the developmental processes are complicated, and where, therefore, errors are most likely to occur. This is shown by the frequency with which epithelioma affects the open-

ings on the surface of the body; the œsophagus where crossed by the left bronchus (the food and air-passage were originally one here); the cardia, pylorus, and commencement of the pyloric portion of the stomach, where change of epithelium occurs; the line of union of the invaginated epiblast and the hind-gut in the rectum; the external os uteri where Müller's ducts opened into the uro-genital sinus. Adenomyomata of the prostate occur at the same spot in the male. Smooth myomata occur almost exclusively in the uterus. The whole uterus is made up of foci of cells awaiting the stimulus of impregnation to great development. Atypical development of one focus may occur without the usual stimulus, and perhaps we should rather expect this when pregnancy has been absent or infrequent. Myomata are commonest in elderly sterile women. Adenomata of the mammæ may be similarly explained.

Heterologous tumours are always so placed that it is possible to see how, by developmental error, some cells which would naturally give rise to the heterologous tissue might have been included in the tumour-germ. Thus dermoids occur near where invaginations of epiblast are normal. Muscle may easily get into the Wolffian bodies from neighbouring muscle plates, and cartilage from the rudiments of vertebræ, &c.

Finally, from so atypical a rudiment, an atypical result would be expected.

Against Cohnheim's view it may be said that nothing is really known of such embryonic remains; that many of the points of complicated development which he mentions are also points of irritation—*e.g.*, the narrowings of the alimentary canal; and that he is obliged to exclude from his class of tumours such cases as epithelioma of scars, of the scrotum in sweeps, of the arm in paraffin-workers, in which irritation plays so obvious a part.

The exciting effect of **increased blood-supply** is evident in many cases—*e.g.*, enlargement of ovarian dermoids at puberty, of tumours of the breast, ovaries, and uterus in pregnancy. This may cause the multiplication of cells

capable of growth; and thus is to be explained the apparent causation of tumours by injuries.

CLASSIFICATION.—Tumours having the most obviously similar structure vary much in their clinical history, whilst others of radically different structure have very similar physical signs and courses. Consequently a clinical classification cannot be constructed, and we are obliged to fall back upon a histological classification based upon the resemblance of every tumour to some normal tissue, adult or embryonic.

For convenience sake, all cysts will be grouped together and remarks on them made at the end of tumours—though the great majority of cysts are not tumours.

CLASSIFICATION OF TUMOURS.

I.—*Type of Fully-Developed Connective-tissues.*

Mesoblast.

Type of fibrous tissue . . .	Fibroma.
„ mucous „ . . .	Myxoma.
„ adipose „ . . .	Lipoma.
„ cartilage	Chondroma.
„ bone	Osteoma.
„ lymphoid „ . . .	Lymphoma. / Lymphangioma.

II.—*Type of Embryonic Connective-tissue.*

The varieties of Sarcoma.

III.—*Type of Higher Tissues.*

Type of muscle	Myoma.
„ nerve	Neuroma.
„ bloodvessels	Angioma.

IV.—*Type of Epithelial Tissues.*

Epiblast and Hypoblast.	Papillæ of skin or mucous membrane	Papilloma.
	Glands	Adenoma. / Carcinoma.

V.—*Teratomata, or Mixed Tumours.*

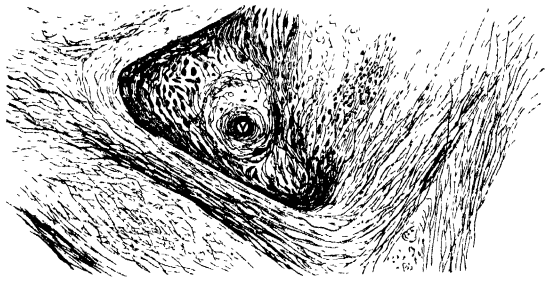
CHAPTER XII.

THE FIBROMATA.

THE Fibromata, fibro-cellular or connective-tissue tumours, are tumours consisting of fibrous tissue.

STRUCTURE.—In structure the fibromata present the same variations as those met with in fibrous tissue. Some of them are composed of firm, dense fibrous tissue, such as constitutes tendons; others are laxer and less fibrous in consistence, more resembling the connective-tissue of the cutis. The fibres, which constitute the chief part of the growth, are more or less closely interlaced, and are distributed without any definite arrangement, or grouped

FIG. 31.



Section of a Fibrous Tumour from the Skin.—In the neighbourhood of the cut bloodvessel v are seen some cells; also fibres cut transversely. × 200 and reduced ½.

in bundles of various sizes. They are sometimes arranged concentrically around the bloodvessels. (Fig. 31.) Yellow elastic fibres are but very rarely met with. The cells, like those of normal fibrous tissue, are generally few in number, and are usually most abundant around the vessels. They are minute, spindle-shaped, fusiform, or

stellate bodies, the latter having processes of varying length, which communicate with similar processes from neighbouring cells. They are often so small and indistinct in the fresh specimen as to become visible only after the addition of dilute acetic acid. These cells in size and number vary with the rapidity of growth—the slower the growth and the more fibrous the tissue, the flatter and less numerous are the cells.

The fibromata usually contain but few bloodvessels. In the softer growths, however, these are often more numerous. Dilated veins sometimes form a cavernous network, the walls of which are firmly united to the tissue of the tumour, so that when divided or ruptured they are unable to retract or collapse, and profuse hæmorrhage may ensue.

DEVELOPMENT. — The fibromata originate from connective-tissue, either from the cutis or subcutaneous connective-tissue, from the submucous or subserous tissue, from fasciæ, the periosteum, the neurilemma, or from the connective-tissue of organs. In the earliest stages of their growth the cells are more numerous than when development is complete. (See p. 118.)

SECONDARY CHANGES.—Of these, partial mucoid softening and calcification are the most common. Ulceration also sometimes occurs in those growths which are situated in the skin and submucous tissues.

VARIETIES.—Fibrous tumours present some variations in their characters, which depend for the most part upon the tissue from which they grow. Two classes may be distinguished:—

1. **Soft Fibromata.**—These consist of the looser and less dense form of fibrous tissue. They are met with as diffused growths in the subcutaneous and submucous tissue. In the former situation they often form large pedunculated and non-encapsuled tumours, which are commonly known as **wens**. These are sometimes multiple. A similar growth of subcutaneous tissue is met with in **Molluscum Fibrosum.** In this disease the large

masses which hang down from the thighs, buttocks, and other situations consist simply of loose fibrous tissue. They often contain numerous large bloodvessels, so that their removal may lead to dangerous hæmorrhage.

In addition to these diffused growths, more circumscribed and **encapsuled** fibrous tumours of the soft variety are occasionally met with growing from the scalp, scrotum, labium, intermuscular septa, and other situations.

2. **Firm Fibromata.**—These are composed of dense fibrous tissue, like that in tendons. They are firm, hard, encapsuled tumours, presenting on section a greyish-white, glistening, fibrous appearance. These tumours often occur in connection with bone, especially with the upper and lower jaws, originating either in the centre of the bone, or from the periosteum. Growing from the periosteum of the alveolus they constitute simple fibrous **epulis**. They are met with also in the nose, where they form one variety of **nasal polypus.** It is in these firm fibrous growths that the veins form the cavernous spaces already alluded to.

Another variety of firm fibrous tumour grows in connection with nerves, and is often described as **neuroma**. True neuromata, however—*i.e.*, new formations of nerve-tissue—are among the rarest forms of new formations. These fibrous growths most frequently occur in connection with the superficial nerves. They grow from the neurilemma, and as they increase in size the nerve-fibres become expanded over them. They are very firm rounded tumours, and are frequently multiple and hereditary.

Some old tumours of the uterus are almost or quite pure fibromata; but the so-called uterine fibroids are in most cases overgrowths of the involuntary muscular tissue of the organ, and will therefore be considered with the *Myomata, p. 170.*

CLINICAL CHARACTERS. — *Clinically the fibromata are perfectly innocent. They grow slowly, and have* no tendency to recur locally after removal.

PSAMMOMA.

This is perhaps the best place to allude to a rare form of growth occasionally met with in the brain and its membranes, which is known as Psammoma. The most characteristic feature of this growth is that it consists largely of calcareous particles. These are contained in the concentric bodies already described as the corpora amylacea, where they give rise to the so-called "brain-sand"—hence the name of the growth. The calcified corpora amylacea are held together by a varying quantity of loose fibrous, or highly cellular, or mucous tissue containing vessels.

Psammoma is usually met with growing from the pineal gland, the membranes of the brain, or the choroid plexus. In the latter situation it often contains numerous cysts. It is of no pathological importance except when of sufficiently large size to produce symptoms from pressure.

CHAPTER XIII.

THE MYXOMATA.

The Myxomata are tumours consisting of mucous tissue. Mucous tissue is connective-tissue, of which the intercellular substance is translucent, homogeneous, and jelly-like, contains much fluid, and yields mucin. Physiologically, this tissue is met with in two forms :—one, as in the vitreous body of the eye, in which the cells are roundish and isolated ; the other, as in the umbilical cord, in which the cells are fusiform or stellate, and give off fine prolongations, which anastomose with one another. The connective-tissues in their embryonic condition, as stated when describing "mucoid degeneration," possess an intercellular substance containing large quantities of mucin. This is especially the case with the tissue which subsequently becomes adipose. New formations may

undergo a mucoid change, and thus closely resemble in their physical and chemical characters the myxomata; but a myxoma consists of mucous tissue from the first. The myxomata are thus very closely allied to the sarcomata, and by many are included in the same class of new formations.

FIG. 32.

Myxoma.—A minute piece of a myxoma of the arm, showing the characteristic branched anastomosing cells. There are also a few leucocytes, and one or two spindle-shaped elements. × 200.

STRUCTURE.—The cells present the two varieties met with in the physiological tissues. The majority are angular and stellate, with long anastomosing prolongations; others are isolated, and fusiform, oval, or spherical in shape. (Fig. 32.) They usually possess one, in some cases two distinct nuclei. Their contour is very indistinct, owing to the refracting nature of the intercellular substance. The latter is very abundant, perfectly homogeneous, of a soft gelatiniform viscid consistence, and yields large quantities of mucin: in it are a varying number of amœboid cells. The bloodvessels, which are not numerous, are readily visible and easily isolated. A few elastic fibres are sometimes seen between the cells.

DEVELOPMENT.—The myxomata always originate from embryonic connective-tissue, which does not advance

beyond the mucous stage of normal development. Adipose tissue is their favourite seat.

SECONDARY CHANGES. — Of these the most common is rupture of the capillaries, hæmorrhage, and the formation of sanguineous cysts; this, however, is less frequent than in the sarcomata. The cells themselves may undergo mucoid or fatty degeneration, and thus be destroyed: this is usually accompanied by liquefaction of the intercellular substance. The growth may inflame, ulcerate, and necrose.

VARIETIES.—The varieties of myxoma depend principally upon its combination with other growths; a pure myxoma is unusual. The most common is a combination with lipoma. Combinations also with sarcoma, fibroma, chondroma, and adenoma, are met with.

PHYSICAL CHARACTERS, &c.—The myxomata are of a peculiar soft gelatiniform consistence, and of a pale greyish or reddish-white colour. Their cut surface yields a tenacious mucilaginous liquid, in which may be seen the cellular elements of the growth. They are usually separated from the surrounding structures by a very thin fibrous capsule, fine prolongations from which divide the growth into lobules of various sizes. In exceptional cases they may increase by the continuous invasion of surrounding tissues. They are most frequently met with in the later periods of life, and are most common in subcutaneous and subserous fat, submucous and intermuscular tissue. They grow also from periosteum and medulla of bone, from the connective-tissue of organs (especially the breast), and from the perineurium of nerves, forming one variety of "neuroma." They may grow also from the placenta, constituting the "uterine hydatids." When situated in superficial parts they may become pedunculated; in the submucous tissue of the nose they constitute one form of nasal polypus. In the skin they are often papillary.

CLINICAL CHARACTERS.—Clinically the myxomata are for the most part benign growths. Their growth

is usually slow, but they may attain an enormous size. If completely removed they rarely recur. Sometimes, however, they recur locally after removal, but they probably never reproduce themselves in internal organs. In speaking of their malignancy, their occasional association with sarcoma must be borne in mind.

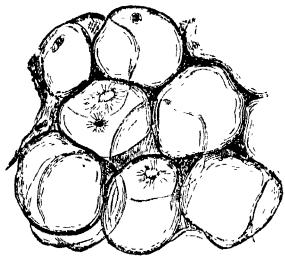
CHAPTER XIV.

THE LIPOMATA.

A GENERAL new formation of adipose tissue, constituting **obesity,** has already been described under "fatty infiltration." A localised and circumscribed formation constitutes a **lipoma,** or fatty tumour.

STRUCTURE.—The lipomata resemble in their structure adipose tissue. (Fig. 33.) They consist of cells containing fat, and a variable quantity of common connective-tissue. The cells are like those of adipose tissue, though usually somewhat larger. The nucleus and protoplasm are so compressed against the cell-wall by the fluid contents, that they are readily visible only when the cell is atrophied and contains less fat. (See Fig. 4*a*.) Connective-tissue, which, varying much in amount, unites the cells in masses or lobules which are larger than normal, forms in most cases around the tumour a thin capsule which adheres more firmly to surrounding parts than to the tumour; so the latter, in most cases, "shells out" easily. Bloodvessels are distributed in the fibrous septa. Mucous tissue is often associated with the fatty (myxo-lipoma).

FIG. 33.



Lipoma. Some of the cells contain crystallised fatty acids. × 200.

DEVELOPMENT.—The lipomata grow from connective-tissue. Adipose tissue, it must be remembered, is merely connective-tissue containing numerous cells which are infiltrated with fat; and its growth consists, either in the infiltration of more of these cells, or in a proliferation of the cells, and an accumulation of fat in those newly developed. A lipoma in the same way originates by a localised proliferation of cells, which, as they are produced, become infiltrated with fat. The growth of these tumours is always very slow.

SECONDARY CHANGES.—Secondary changes in the lipomata are not common; their fibrous septa may, however, become calcified, or even ossified. Softening may occur also from a mucoid change. Inflammation is rare; but when large and situated in the subcutaneous tissue the skin over them may become adherent, and ulceration and necrosis of the tumour occur.

PHYSICAL CHARACTERS, &c.—The situation of the lipomata is almost co-extensive with that of adipose and connective tissue. They occur most frequently in the subcutaneous tissue of the trunk, especially of the back and abdominal wall; sometimes in intermuscular septa, subsynovial and subserous tissues; and occasionally also in the submucous tissue of the stomach and intestines, and even in internal organs where there is normally no fat. They sometimes attain an enormous size. They are more or less lobulated, and are usually surrounded by a fibrous capsule, which separates them from the adjacent structures. They move freely over the deep fascia when subcutaneous; but often the attempt to raise the skin from them causes it to dimple. On section they present the ordinary appearance of adipose tissue. Their consistence and adhesion to the capsule vary with the amount of fibrous tissue which they contain. They are usually single, but not infrequently multiple and hereditary. In their growth they occasionally become pedunculated.

CLINICAL CHARACTERS.—Clinically, the lipomata are perfectly innocent.

CHAPTER XV

CHONDROMATA.

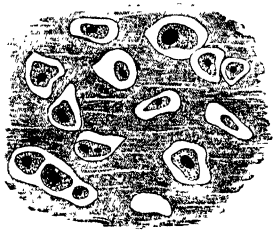
The Chondromata are tumours histologically resembling cartilage.

STRUCTURE.—Like cartilage they consist of cells and an intercellular substance, which present all the variations observed in the normal tissue. The intercellular substance may be hyaline, faintly or distinctly fibrous, or mucoid. When fibrous, the fibres may be arranged like those of fibro-cartilage, or more or less concentrically around the cells, as in the reticular cartilages of the ear and larynx. (Fig. 34.) When hyaline or mucoid, it is sometimes quite soft in consistence. The cells may be very numerous, or few in proportion to the matrix. In the hyaline forms they are usually large and round or oval (Fig. 35); in the fibrous forms they are often smaller and even somewhat spindle-shaped, more resembling those of connective-tissue; and in the rarer mucoid forms they are more commonly stellate and branched, like the transitional cells at the edge of articular cartilages where the synovial membrane ends. They are either single or arranged in groups, and are usually surrounded by a capsule of fibrous tissue, which is often very indistinct. They enclose one or more nuclei and slightly granular contents; sometimes a cell-wall cannot be distinguished.

Fig. 34.

Fibrous Chondroma. × 200.

Fig. 35.



Hyaline Chondroma. × 200.

A large growth is usually divided into several lobes by bands of fibrous tissue, in which are contained the blood-vessels. These lobes are often very distinct, so that the growth appears to be made up of several separate tumours. Fibrous tissue in most cases also encapsules the growth, and separates it from the surrounding structures; but sometimes this capsule is absent, and the tumour is surrounded by a zone of embryonic cells, which infiltrate the adjacent tissues.

DEVELOPMENT.—The chondromata most frequently originate from common connective-tissue and bone, very rarely from cartilage. Cartilage itself, and especially fibro-cartilage, is very closely allied to common connective-tissue. It grows from the deeper layers of the peri-chondrium, which proliferate and form an embryonic tissue; the young cells become cartilage-cells, and these probably form the matrix, which is either homogeneous or fibrillated, constituting in the one case hyaline, and in the other fibro-cartilage. The development of chon-droma from connective-tissue is precisely similar to the physiological progress.

In the development of chrondroma from osseous tissue, the medulla is the source of the new growth. This pro-liferates and forms embryonic tissue, which absorbs tra-beculæ and occupies the resulting space; cartilage is formed from it, as above. The mass gradually increases, a layer of fibrous tissue is formed around it, and further growth takes place from the tissue of the capsule. Vir-chow has shown that islands of cartilage not uncommonly remain in the shafts of bones, and has rendered it pro-bable that many chondromata spring from them. They generally begin before the ossification of the epiphyses, whilst the bone is actively growing and vascular.

Lastly, cartilaginous growths may originate from car-tilage itself. These are sometimes seen on the surface of the articular cartilages, in the larynx and trachea, and on the costal and intervertebral cartilages. They are simply local overgrowths from pre-existing cartilage.

They rarely attain a large size, and in structure and physical characters more closely resemble normal cartilage than the other forms of chondroma. They are usually described as **ecchondroses,** and must be distinguished from the other forms of cartilaginous tumour.

SECONDARY CHANGES.—Calcification is the most common, because it is frequent in the commonest chondromata—those of the phalanges and metacarpals of the hands. It spreads from many centres, commencing in the capsules, and then involving the intercellular substance. Ossification also occurs, especially in the chondromata which grow near the junctions of the epiphyses and shafts of long bones; these ossify as they grow, and form the pedunculated exostosis. So also does the common sub-ungual exostosis of the great toe, which is generally an ossifying chondroma. Fatty degeneration and mucoid softening are common changes, and may lead to the formation of large softened masses which present the appearance of cysts. In rare cases the skin covering the tumour ulcerates, and a fungating mass protrudes.

VARIETIES.—The varieties of chondroma depend mainly upon the nature of the intercellular substance. There are thus hyaline, fibrous, and mucoid chondromata; these, however, are usually combined in various degrees in the same tumour. As a rule, those originating from the medulla of bone are of the hyaline and mucoid class, whilst those originating from connective-tissue in other situations are more frequently fibrous. The rapidly growing fibrous forms approach very closely to the sarcomata, the mucoid forms to the myxomata; and these two kinds of growth are often associated in the same tumour. As above stated, chondromata are rarely homologous.

A variety of chondroma has been described under the name of **osteo-chondroma,** which in structure more closely resembles bone than cartilage. It consists of a tissue similar to that met with between the periosteum and bone in rickets, which, from its resemblance to osseous,

has been called **osteoid** tissue. This tissue requires only calcifying to become true bone. Like bone, it is made up of trabeculæ and medullary spaces; but the trabeculæ, instead of bone-corpuscles and lamellæ, consist of small angular cells without a capsule, situated in an obscurely fibrillated matrix, which in part is calcified. The medullary spaces contain a fibrous stroma and many blood-vessels. The osteo-chondromata, although consisting mainly of this osteoid tissue, contain also a small proportion of cartilage. They originate beneath the periosteum, their common seat being the ends of the long bones. Their growth is very rapid, and they often attain an enormous size. They are much more freely supplied with bloodvessels than the ordinary chondromata, and hence they are much less frequently the seats of retrogressive changes. They are especially prone to become ossified and converted into true bone.

PHYSICAL CHARACTERS, &c.—The chondromata occur most frequently in early life. About three-fourths of them are met with in the osseous system, where they grow either centrally or sub-periosteally. Their favourite seats are the fingers and toes, the lower end of the femur, and the upper of the humerus and tibia. Most of the remaining fourth occur in the parotid gland and in the testicle. Cohnheim suggests as the source of this in the parotid an aberrant bit of the cartilaginous rudiment of the jaw; Virchow, a piece of the cartilage of the pinna. In the testis a portion of the rudiment of a vertebra may have been included. They occasionally occur in the inter-muscular septa, in the subcutaneous tissue of the breast, and in the lungs. They are usually single, except when occurring on the fingers and toes, in which situations they are more frequently multiple. They consist of a single tumour, or of several smaller tumours held together by fibrous tissue. The more slowly-growing chondromata are hard, smooth, elastic tumours, often lobulated, and seldom exceeding the size of an orange. Less frequently these tumours grow very

rapidly, are soft in consistence, and attain a large size. Such growths often start from the pelvic bones or ribs.

CLINICAL CHARACTERS.—The chondromata must for the most part be regarded as innocent growths. They are usually encapsuled, and in most cases produce merely local effects, although these, from the parts involved and the rapidity of the growth, are often very injurious. The softer forms, however, and especially those which occur in the medulla of bone and in the glands, occasionally exhibit malignant characters. These grow the most rapidly, and are often not limited by a fibrous capsule, but surrounded by a zone of embryonic tissue. They consist of very vascular spindle-celled tissue, together with well-developed hyaline cartilage, and are spoken of as chondro-sarcomata. Such tumours tend to recur locally after removal, and in rare cases also infect the lymphatic glands, and are reproduced in the lungs.

CHAPTER XVI.

THE OSTEOMATA.

THE Osteomata are tumours resembling in structure normal bone.

STRUCTURE.—The bone may be exceedingly dense, or very open and cancellous; but all intermediate grades occur.

VARIETIES.—Two classes are made from the above variations in density.

1. **The Eburnated or Ivory Osteomata.**—These consist of dense ivory-like bone; the lamellæ are arranged concentrically and parallel to the surface of the tumour; cancellous tissue is absent, and Haversian canals are few and narrow. Some specimens are less dense, the Haversian canals being as numerous as in ordinary compact bone, but less regularly arranged.

The Cancellous or Spongy Osteomata.—These consist of cancellous, surrounded by a thin layer of compact, bone. The medullary spaces may contain embryonic, fibrous, or fatty tissue.

DEVELOPMENT.—The formation of bone may, as in normal development, take place directly from fibrous tissue, or be preceded by the development of cartilage: thus we get **fibrous** and **cartilaginous** exostoses. The ivory exostoses of the skull are examples of the former, the spongy exostoses near the epiphyses of long bones of the latter. A growing spongy exostosis is covered by a layer of cartilage; when this ossifies, growth ceases.

SEATS, PHYSICAL CHARACTERS, &c.—Bony tumours are much commoner in connection with bone (homologous) than elsewhere (heterologous), growing from the periosteum, endosteum, or from persistent islands of cartilage. They generally project from the surface (exostosis); but rarely form within the medullary canals (enostosis).

The **homologous osteomata** or **exostoses** growing from periosteum are almost always dense and eburnated, and occur most frequently on the external and internal surfaces of the skull: the orbit is an especially favourite seat. They are met with also on the scapula, pelvis, and on the upper and lower jaws. In the last-named situation they may grow from the dental periosteum. There is usually a line of demarcation between them and the subjacent bone, the new tissue of the tumour being distinct from the compact tissue of the bone. The periosteum from which they grow covers them, and is continuous with that of the old bone. Such growths are smooth, low, rounded, and wide-based.

The homologous exostoses growing from cartilage occur at the ends of the long bones close to the line of junction of epiphysis and shaft. In structure they are much more cancellous than the periosteal growths, and their outline is less regular; but they are prominent and pedunculated generally. The medullary osteomata—or

more properly, **enostoses**—are the least frequent: they originate in the medullary tissue.

Heterologous osteomata originate apart from bone, growing from connective tissue. They are very rare as primary growths. They have been described as occurring in the subcutaneous tissue; but Malherbe has shown reason for believing that such growths are really sebaceous adenomata of which the stroma is ossified. Bony tumours have very rarely been formed in the brain and cerebellum. Parts of fibromata, lipomata and chondromata may ossify. The secondary growths of ossifying sarcomata in connection with bone, often ossify.

The osteomata being the result of the ossification of newly formed connective tissue, which is not a product of inflammation, must be separated from simple ossification of normally existing tissues—such as rib, laryngeal or bronchial cartilages, insertions of muscles (rider's bone in adductor longus and the like), and membranes of the brain; and also from ossifications of inflammatory tissue—such as nodes or general thickenings of bones, the sharp stalactitic processes which may grow round a carious joint or surface of bone, and the smooth round prominences which form round a joint in rheumatoid arthritis. They must be distinguished from calcareous deposits, in which there is no bone formed (see "Calcareous Degeneration").

SECONDARY CHANGES.—Osteomata may inflame, become carious or necrose. The latter is most likely to occur in ivory exostoses, causing their separation and cure.

CLINICAL CHARACTERS.—The osteomata are perfectly innocent tumours. Their growth is very slow. They rarely attain a large size. They are often hereditary and multiple, in which case they usually occur in early life. Osseous growths which exhibit malignant characters, are chondromata or sarcomata which have undergone partial ossification. From these, true osteomata must be carefully distinguished (see "Osteoid Sarcoma").

CHAPTER XVII.

THE LYMPHOMATA.

THE Lymphomata are new formations consisting of lymphoid, or as it is sometimes called, adenoid tissue (His). Lymphoid tissue is now known to have a much more general distribution than was formerly supposed. It not only constitutes the follicles of the lymphatic glands and the Malpighian corpuscles of the spleen, but also Peyer's glands and the solitary glands of the intestines, the follicles of the pharynx and tonsils, the thymus gland, and the trachoma glands of the conjunctiva. Recently it has been found to exist also in many other situations, as around the blood-vessels of the pia mater and of other parts, in the neighbourhood of the smallest bronchi, in the pleura immediately beneath its endothelium, in the peritoneum, in the mucous membrane of the alimentary canal, and in the medulla of bone.

STRUCTURE.—Lymphoid tissue, wherever it exists, possesses the same general structure, and the follicle of a lymphatic gland may be taken as the type not only of the physiological tissue but also of the pathological growths.

This tissue consists of a delicate reticulum, within the meshes of which are numerous lymph-corpuscles. The reticulum is a close network of very fine fibrils, the meshes of which are only sufficiently large to enclose a few, or even a single corpuscle, in each. The fibrils usually present a more or less homogeneous appearance, and nuclei are sometimes to be distinguished at the angles of the network. The lymph-corpuscles, which constitute the greater part of the tissue, can in most cases be readily removed from the meshes of the reticulum by the agitation of thin sections in water. They are identical in their characters with the white cells of the blood. As usually seen after death, they are spheroidal, pale, semi-transparent bodies, varying considerably in size, and pre-

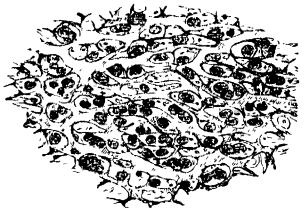
senting slight differences in structure. Some are granular, and appear to possess no nucleus; in others, a distinct, simple, or compound nucleus is visible, which is usually also granular; others again are much larger, and contain two or even three nuclei. (Fig. 36.)

The histological and physical characters of the lymphomata, however, vary considerably, according to the rapidity of their development. In the rapidly growing forms the proportion of cells is very great, and many of these are larger than those normally met with in lymphatic glands, containing two, or even more, nuclei; they are of a greyish-white colour, and soft brain-like consistence—much like encephaloid cancer—and yield abundance of milky juice. They may reach a great size. The more slowly growing tumours, on the other hand, are less richly cellular, and the larger cell-forms are almost entirely wanting; the reticulum constitutes a more prominent part of the growth (Fig. 37), and instead of being exceedingly delicate, is

FIG. 36.

Cells from a Lymphatic Growth in the Liver.—Those to the left are the ordinary lymph-corpuscles, which constituted the greater part of the growth. To the right are some of the larger elements. × 350.

FIG. 37.



Lymphoma.—Section of a firm lymphoma of the mediastinum. Showing a very thickened reticulum, within the meshes of which the lymphoid cells are grouped. × 200.

much coarser and forms a network of broad homogeneous or slightly fibrillated bands. As the reticulum increases the lymph-corpuscles gradually diminish in number and become arranged in smaller groups within its meshes. (Fig. 37.) Such growths are much harder than the

more rapidly growing ones; they are sometimes exceedingly dense. They are rarely very large. These variations in the proportion of cells and stroma are precisely analogous to those met with in lymphatic glands as the result of acute and chronic inflammation (see "Inflammation of Lymphatic Structures"); but in many cases the relation between cells and stroma remains normal, as in hyperplasia.

DEVELOPMENT.—The lymphomata originate from lymphoid tissue, being simply uniform overgrowths of pre-existing lymphatic structures—mainly of the lymphatic glands. They are, therefore, usually homologous. They may, however, be heterologous, either owing to the new tissue extending considerably beyond the confines of the old, or to its origin in situations where lymphoid tissue is not present normally. This latter condition obtains in Hodgkin's disease, and in certain forms of lymphoma which are malignant.

In some cases of round-celled sarcoma, which may originate in any connective tissue, the matrix undergoes development into a network; the growths spread and generalise like ordinary sarcomata, and are called **lympho-sarcomata**. They may originate in lymphatic glands.

In considering the development of these growths it must be borne in mind that enlargements of lymphatic structures are most frequently of an inflammatory nature, being due to some injury; and histologically, as already indicated, there is but little difference between these inflammatory growths and lymphomatous tumours. The inflammatory growths, however, tend to subside, the tumours continuously to increase. Further, the development of the tumours may, like that of the inflammatory growths, be determined by some injury, the injury producing perhaps some inflammation and enlargement of the gland, but this instead of subsiding continues more or less rapidly to increase. (See "Etiology of Tumours.")

SECONDARY CHANGES.—The lymphomata do not

undergo marked retrograde changes. There is no fatty degeneration, caseation, or softening, such as occurs in scrofulous glands.

CLINICAL CHARACTERS.—Clinically, the lymphomata are, for the most part, perfectly innocent tumours. They originate most frequently in the lymphatic glands, the gland undergoing a continuous increase in size. Sometimes, as already stated, the enlargement of the glands appears in the first place to be of an inflammatory nature and to result from some irritation, but upon this being removed the glands, instead of subsiding, continue to increase. In most cases, however, no such source of irritation is discoverable. The glands which are especially prone to this disease, are the cervical, the submaxillary, the axillary, the inguinal, the bronchial and mediastinal, and the abdominal glands. Usually only a single gland, or a single group of glands, is affected; sometimes, however, the growth is more general. As the glands enlarge, they gradually unite, so that ultimately they may form very large lobulated tumours. When occurring in the mediastinum they may invade one or both lungs, and they constitute here the most common form of mediastinal tumour (so-called "Thoracic Cancer"). The lymphatic structures in the intestine may in the same way become enlarged, and project, so as to form polypi.

The lymphomata occasionally, however, exhibit malignant properties. This is especially the case in those richly cellular, soft, rapidly growing forms which are sometimes met with. Such growths may rapidly infiltrate the surrounding structures, involve the neighbouring lymphatic glands, and even infect distant parts. To these malignant forms the term **lymphadenoma** is sometimes applied. They correspond with Virchow's lympho-sarcoma.

In the condition known as "Hodgkin's Disease," and in leukæmia, lymphomatous growths are met with in various parts of the body.

HODGKIN'S DISEASE.

This disease is characterised by the enlargement of the lymphatic glands in various parts of the body, together with the development of lymphatic growths in internal organs, especially in the spleen; by a diminution in the number of red corpuscles in the blood; and by progressive anæmia. The new growths are precisely similar, histologically, to lymphoma. The disease was described by Hodgkin, Bright, Wilks, and Trousseau, and is called, after the first-named of these observers, "Hodgkin's Disease;" Trousseau designated it "Adénie;" it is also known as "Anæmia Lymphatica." It is allied to leukæmia, but differs essentially from it in this respect, that the new formation of lymphatic tissue is not associated with any notable increase in the number of the white corpuscles in the blood. (See "Leukæmia.")

The lymphatic glands are usually the earliest seats of the new growth. At first only a single group of glands may be enlarged; subsequently, however, the process becomes more general, and the glands throughout the whole body may be more or less involved. The groups of glands most frequently affected, in the order of their frequency, are the cervical, the axillary, the inguinal, the retro-peritoneal, the bronchial, the mediastinal, and the mesenteric. The new growth, which in the earlier stages is limited to the glands, gradually breaks through the capsules, so that the enlarged glands become confluent, and form large lobulated masses. The growth may also extend still further beyond the confines of the gland and invade and infiltrate the adjacent structures.

This new growth of lymphatic tissue, which commences in and often extends beyond the confines of the lymphatic glands, is ultimately followed by the formation of lymphatic growths in various internal organs, but more especially in the spleen. The spleen is affected in a large proportion of cases. Here the new growth originates in the Malpighian bodies, and so gives rise to disseminated

nodules. These vary in size from minute points to masses as large as a hazel-nut or walnut. They are usually more or less irregular in shape, of a greyish or yellowish-white colour, firmer in consistence than the splenic tissue, and not encapsuled. In addition to these, wedge-shaped infarctions surrounded by a zone of hyperæmia are sometimes met with, similar to those which are often seen in leukæmia. The spleen itself is increased in size, although rarely very considerably so; and its capsule is usually thickened, and often adherent to adjacent organs. In quite exceptional cases the spleen is not the seat of these disseminated growths, but is simply uniformly enlarged, like the leukæmic spleen.

The liver, kidneys, alimentary canal, medulla of bone, lungs, and subcutaneous tissue may all become involved, the new growths occurring either as nodules of various sizes scattered through the organs, or in a more infiltrated form, like many of those met with in leukæmia.

Histologically, the new growths are precisely similar to the lymphomata, and like these present differences in the relative proportions of cells and stroma, the richly cellular forms being soft and pulpy, whilst those in which the stroma is more abundant are firmer and more fibrous in consistence. Retrogressive changes rarely occur.

With regard to the pathology of the disease, it is undoubtedly obscure. The development of the new growths cannot in most cases be regarded as the result of infection from a primary centre, as the process is, for the most part, confined to the lymphatic structures, and many and widely distant groups are often simultaneously involved. The disease thus appears to occupy a different pathological position to that of the malignant tumours. It is probable that there is some special weakness of the lymphatic structures generally which renders them prone to undergo these active developmental changes, the process being determined by some constitutional state or by some local injury of the glands. The progressive anæmia which accompanies, but does not precede, the gland-

affection, is due to the progressive implication of the lymphatic structures and to the consequent interference with the formation of the blood-corpuscles.

LEUKÆMIA.

In leukæmia, as in Hodgkin's disease, there is usually a development of lymphomatous tissue in various organs. The disease, however, is characterised by the large increase in the number of white corpuscles in the blood, and in the majority of cases by enlargement of the spleen. It is this alteration in the blood which gives leukæmia its distinctive characters—hence its name. The disease will be considered subsequently, when treating of "Diseases of the Blood."

THE LYMPHANGIOMATA.

The Lymphangiomata are tumours consisting of lymphatic vessels which are larger than normal; but it is doubtful what shares simple dilatation and new formation of lymphatic vessels take. The divisions are the same as those of angioma—simple and cavernous lymphangioma. A section of the latter would scarcely be distinguishable from one of cavernous nævus (see Fig. 49), except by the contents of the spaces. There is generally fat in the stroma.

Each kind may be congenital or acquired. Congenital dilatations are found in the tongue (makro-glossia), lip (makro-cheilia), and labium, causing hypertrophy of the parts; and also elsewhere in the skin.

Acquired dilatation is not rare in the skin, especially of the thigh and thorax, forming tumours sometimes as large as an orange in the subcutaneous tissue; dangerous loss of lymph may occur from rupture of a vessel. Fibroid thickening of the parts from which lymphatics pass to the tumour may occur.

CHAPTER XVIII.

THE SARCOMATA.

THE Sarcomata are tumours consisting of embryonic connective tissue. Of these there are several varieties, depending upon the size and configuration of the cells, and the nature of the intercellular substance. They include what have generally been known in this country as **fibro-plastic, fibro-nucleated, recurrent fibroid,** and **myeloid** tumours. Many growths formerly described as "cancers" also belong to this class of new formations.

Connective tissue in its most immature state differs from the fully developed tissue in consisting almost entirely of small round cells, whilst its intercellular substance is wholly soft and amorphous. This is the common condition of connective tissue in the primary stages of *all rapid formative processes*, as already described when *speaking of it as the tissue from which many tumours of* the connective-tissue class originate. (See "Development of Tumours.")

In the normal development of this embryonic into mature connective tissue, the cells diminish in number, many of them assume a spindle shape, and the intercellular substance fibrillates. Similar changes are seen in inflammatory conditions of connective tissue. In the sarcomata, however, the connective tissue retains the embryonic state, and throughout their growth there is a progressive formation of embryonic tissue. Not uncommonly the process of development leads in parts of the tumour to the formation of a more highly developed structure, as fibrous tissue, cartilage, or bone, so that a mixed form of tumour is produced.

STRUCTURE.—The sarcomata may thus be defined as tumours consisting of connective tissue which throughout its growth more or less retains the embryonic type,

in so far at least that cells predominate over intercellular substance. The **cells**, which constitute nearly the whole of the growth, consist for the most part of masses of nucleated protoplasm, and rarely possess a limiting membrane. They vary much in size and form; and though in a tumour one form usually predominates, all may generally be found by search (Cornil and Ranvier). Often the different forms are much mixed in the same growth. There are three principal varieties—**round, fusiform,** and **myeloid** cells.

The **round** cells are many of them indistinguishable from lymph-cells or white blood-corpuscles. Others are somewhat larger and contain an indistinct nucleus with one or more bright nucleoli: these more closely resemble the cells of a granulation.

The **fusiform** or **spindle-shaped** cells are the so-called "fibro-plastic cells." (Fig 38.) They are long narrow cells, terminating at each end in a fine prolongation. Some of them may be broader, approaching the epithelial type; others more or less stellate. They are sometimes slightly granular, and they enclose a long oval nucleus, with or without nucleoli. In size they vary considerably. These cells represent a higher state of development than the round cells, resembling those met with in embryonic tissue which is in the process of forming mature connective tissue.

FIG. 38.

Cells from a Spindle-celled Sarcoma. × 350.

The **myeloid**, or mother-cells, are much larger than either of the preceding, and are analogous to the cells met with in the medulla of the fœtal bone. (See Fig. 47.) They are large irregular masses of nucleated protoplasm, generally roughly spherical, and often possessing numerous offshoots. They are finely granular, and contain several

round or roundly-oval nuclei, each with one or more bright nucleoli. The nuclei may be exceedingly numerous, one cell containing as many as thirty. Both cells and nuclei vary considerably in size.

An **intercellular substance** exists in the sarcomata, intervening between all cells as in ordinary connective tissues. But it may be absent as in endothelium, lymphatic epithelium, &c. It is usually small in quantity, the cells lying almost in apposition. It may be perfectly fluid and homogeneous, or firmer and granular, or more or less fibrillated. Chemically it yields albumen, gelatin, or mucin. On its amount and nature the consistence of the growth depends.

The **blood-vessels** are usually very numerous, and are either in direct contact with the cells, or separated from them by a little fibrillated tissue. Their distribution is very irregular, and their walls are often formed by the cells of the tumour. Hence the ease with which early generalisation can occur, and the frequency with which rupture and extravasation of blood take place. Lymphatics are not known.

DEVELOPMENT.—The sarcomata always originate from connective tissue, and may occur wherever connective tissue is present. Congenital warts and pigment-spots often serve as their starting-point in later life (p. 129). They increase by the continuous invasion of their connective-tissue matrix, so that no line of demarcation exists between the two. They frequently invade also other tissues, the elements of the growth extending for some distance into the surrounding structures. This infiltrating tendency of the sarcomata varies considerably in the different varieties, being much more marked in the round-celled than in the small spindle-celled and myeloid growths. A circumscribed growth is less common, but a sarcoma may acquire a capsule by stretching around itself the connective tissue of the organ in which it originates. The very varying malignancy of tumours having the structure of sarcomata is a main point with Cohnheim in

establishing the necessity for diminished physiological resistance before malignancy can be manifested (p. 125).

SECONDARY CHANGES.—The most important of these is fatty degeneration. This always occurs to a greater or less extent in the older portions of the growth, causing softening, or the production of cyst-like cavities. It is frequently associated with rupture of the blood-vessels and hæmorrhage : the latter may give rise to the formation of sanguineous cysts. (See "Blood-Cysts, p. 168.") Calcification (Fig. 42), ossification (Fig. 43), and mucoid degeneration are less common. The occurrence of calcification, ossification, and pigmentation is influenced by the predisposition of the matrix from which the growth is produced :—thus, calcification and ossification are more prone to occur in tumours originating in connection with bone, pigmentation in those originating from the cutis or eyeball.

VARIETIES.—Although all the sarcomata possess the same general characters, they present many histological and clinical differences which may serve as bases for their classification. The occurrence of various secondary changes—pigmentation, mucoid degeneration, and the formation of cysts, impart their respective characters to the growth ; hence **melanotic-sarcoma** and **cystic-sarcoma** have been described as distinct varieties. This is to a certain extent justifiable, inasmuch as sarcomata which have undergone these transformations, in many cases possess the property of reproducing the same characters, when they occur secondarily in other parts. Then, again, as already stated, sarcomatous tumours are sometimes complex in their structure, and are associated with other tissues belonging to the connective-tissue group. A combination of sarcoma with fatty, cartilaginous, osseous, and mucous tissue, is thus not uncommonly met with. This is owing to the embryonic tissue exhibiting a tendency to develop into the different varieties of connective tissue. (See " The Tumours.") The mixed forms—**lipo-sarcoma, chrondro-sarcoma, osteo-sarcoma, myxo-sarcoma,** &c., are thus produced. The following histological classifica-

tion, based upon the three different forms of cells already described, is the one generally adopted. As all the varieties of cells may be found in the same tumour, the *majority* will determine the class to which the growth belongs. If no one form predominates, the growth is called "**mixed-celled.**" The extreme edge must be avoided in examinations, on account of the round-celled growth here which is common to many tumours.

SPINDLE-CELLED SARCOMA.

These tumours, which include the growths described by Paget in this country as "fibro-plastic," and "recurrent fibroid," are the most common of all the sarcomata. They consist of cells mainly spindle-shaped and fusiform, separated by only a little homogeneous or slightly fibrillated intercellular substance. These often form whorls round the vessels. The cells, which contain well-marked oval nuclei, with one or more nucleoli, are arranged in bundles which pass in all directions through the growth, often giving to it a somewhat fibrous appearance. In those portions of the section in which the bundles of spindle elements have been cut transversely, they present the appearance of round cells. The cells vary considerably in size in different tumours, hence the division into **small** and **large** spindle-celled growths.

FIG. 39.

Small Spindle-celled Sarcoma.—From a tumour of the leg. × 200.

Small Spindle-celled Sarcoma.—In these the cells are small, often not more than $\frac{1}{1500}$th inch in length, and the intercellular substance is occasionally imperfectly fibrillated. (Fig. 39.) These growths approach therefore the confines of the fibromata, and histologically they must be regarded as occupying an intermediate place between embryonic and fully-developed connective tissue. They grow from the periosteum, the fasciæ, and from connective

tissue in other parts. They are usually tolerably firm in consistence, of a whitish or pinkish-white colour, and for the most part present, on section, a translucent somewhat fibrillated appearance. They are often encapsuled, much more frequently so than other varieties of sarcoma, but they are very liable to infiltrate the surrounding structures, and to recur locally after removal.

Large Spindle-celled Sarcoma.—The cellular elements in these tumours are much larger than in the preceding. The cells are plumper, and the nuclei and nucleoli are especially prominent, and frequently multiple. (Fig. 40.) The intercellular substance is more scanty, and there is

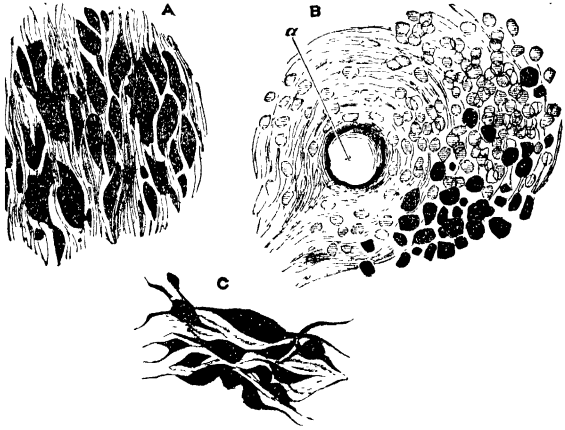
Large Spindle-celled Sarcoma.—To the left—the cells have been separated by teasing, so that their individual forms are apparent; to the right—they are in their natural state of apposition, such as would be seen in a thin section of the tumour. (Virchow.)

a complete absence of any fibrillation. These growths are much softer in consistence than the small-celled variety. They are of a pinkish-white colour, and are often stained by extravasations of blood, and sometimes in parts are almost diffluent from extensive fatty degeneration. They grow rapidly, and are usually exceedingly malignant.

MELANOTIC SARCOMA.—This is a variety of sarcoma in which many of the cells contain granules of dark-coloured pigment, quite distinct from the pigment of extravasated blood. By far the greater number of melanotic tumours are sarcomata, and most of the growths which were formerly described as "melanotic cancers," belong in reality to this class of new formations.

The melanotic sarcomata originate principally in two situations—in the choroid coat of the eye, and in the

FIG. 41.



A Melanotic Sarcoma of the Penis.—A. A thin section showing the general arrangement of the elements. × 200. B. A section from the peripheral part of the growth, showing the "indifferent cells," amongst which are small isolated pigmented elements. At *a*, a blood-vessel is seen. × 200. C. Some of the elements separated by teasing. In these the pigment granules are well seen. × 400.

superficial integuments. In both of these situations pigment is a normal constituent of the tissues, and this tendency of structures normally containing pigment to originate melanotic growths is exceedingly characteristic.

(See "Pigmentary Degeneration.") These tumours usually consist of spindle-shaped cells, and hence they are described in the present section; but in some cases the prevailing type of cell is round or oval. (Fig. 41.) The pigment, which gives to them their distinctive characters, consists of granules of a brownish or dark sepia colour, which are distributed within the cells (Fig. 41, c), and also in the intercellular substance. Frequently, only a very small proportion of the cells are pigmented, whilst in other tumours the pigmentation is much more universal. In all cases, however, a large number of the elements will be found to be quite free from pigment.

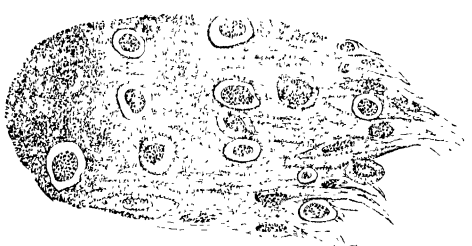
These melanotic tumours are amongst the most malignant of the sarcomatous growths. Although they have comparatively but little tendency to extend locally, they are disseminated by means of the bloodvessels, and occasionally also by the lymphatics, and thus reproduce themselves, often very rapidly, in distant tissues. In doing so, although they almost invariably maintain their melanotic character, the degree of pigmentation of the secondary tumours varies considerably. Whilst many of them may be perfectly black in colour, others may be much paler, and perhaps only streaked with pigment. The secondary growths are soft, usually distinctly circumscribed, and often encapsuled. They may occur in almost every organ of the body—the liver, the spleen, the kidneys, the lungs, the heart, the brain, and spinal cord, and also the lymphatic glands and subcutaneous tissue, may all be simultaneously involved. I have observed that, when occurring in internal organs, the pigmentation is not always limited to the secondary nodules, but that many of the cells proper to the organ itself are filled with granules of similar pigment, which is most abundant in the cells immediately adjacent to the new growth. This pigmentation of the cells of the organ often extends for some distance beyond the confines of the tumour.

OSTEOID SARCOMA.—This, which was often called "osteoid cancer," is a variety of sarcoma (usually spindle-

celled) in which the growth is either more or less calcified, or has partially become converted into true bone. As a primary growth it is met with almost exclusively in connection with bone, growing either from the periosteum or the medulla; but the osteoid characters are usually reproduced in secondary tumours occurring in the lungs and other parts.

Calcification is much more common than true ossification; they may occur separately, but are often combined. Bands and patches of granular appearance, in which the outlines of cells may still be visible, or in which all structure has disappeared, and which stain but

FIG. 42.



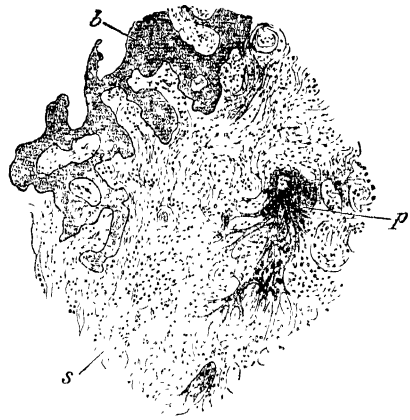
Calcifying Sarcoma.—From a secondary tumour of the lung. Showing the calcification of a spindle-celled growth, and the formation of broad bands of calcified intercellular material enclosing spaces which contain round and oval cells. × 200.

slightly, show where calcification has occurred. (Fig. 42.) In other parts, especially near the bone, spicules having the structure of more or less perfect bone—Haversian canals, lacunæ, and imperfect canaliculi—will be seen penetrating the growth. (Fig. 43.) The spicules are generally vertical to the surface of the bone. In some cases a skeleton of bony spines radiates from the bone through the growth.

Both calcification and ossification may be very complete, only a thin margin of sarcoma-tissue being left unaffected.

In the canals and spaces fibres often develop. A simple osteoma would have cartilage or periosteum on its surface,

FIG. 43.



Ossifying Sarcoma of Lower Jaw.—*s.* Sarcoma-tissue; *b.* new bone, growing from jaw, of which the structure is fairly typical; *p.* point of commencing ossification. Only nuclei of cells are indicated; close to the bone the stroma is very fibrous. × 40.

and would be of much slower growth. It is most important to recognise the difference.

ROUND-CELLED SARCOMA.

This is of softer consistence than the spindle-celled growths, and from its frequent resemblance in physical characters to encephaloid, it is sometimes known as "medullary," "encephaloid," or "soft" sarcoma. Histologically, it is elementary embryonic tissue, consisting mainly of the round cells already described, embedded in a scanty and usually soft, homogeneous, or

finely granular intercellular substance. (Fig. 44.) The cells usually resemble those met with in the most elementary embryonic tissue; less frequently they are larger, and contain large round or oval nuclei, with bright nucleoli. There is an almost complete absence of fusiform cells, and of the partial fibrillation which is so frequent in the more highly developed spindle-celled variety.

FIG. 44.

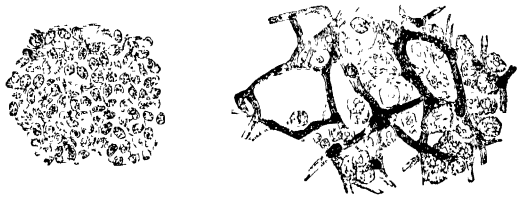
Round-celled Sarcoma.—A thin section of a small round-celled sarcoma of the liver. × 200.

The round-celled sarcomata are of a uniform soft, brain-like consistence, somewhat translucent or opaque, and of a greyish or reddish-white colour. On scraping the cut surface, they yield a juice which is rich in cells. They are exceedingly vascular, the vessels often being dilated and varicose, and, from their liability to rupture, they frequently give rise to ecchymoses and to the formation of sanguineous cysts. (See "Blood-Cysts.") They grow from the cutis, the subcutaneous cellular tissue, the periosteum, the fasciæ, and the connective tissue of organs. They extend rapidly by peripheral growth, infiltrate the surrounding structures, reproduce themselves in internal organs, and often involve the lymphatic glands. From their clinical and physical characters, these tumours are very liable to be confounded with encephaloid cancer:—they are distinguished by the absence of an alveolar stroma, and by the penetration of the intercellular substance between the individual cells.

GLIOMA.—This is a variety of round-celled sarcoma growing from the neuroglia or connective tissue of nerve. It consists of very small round cells, embedded in an exceedingly scanty, homogeneous, granular, or slightly fibrillated intercellular substance. (Fig. 45, *a*.) Some of the cells may possess fine prolongations which, by communicating with one another, form a somewhat reticulated structure. These tumours occur in the grey and white substance

of the brain, in the cranial nerves, and in the retina. In the retina they usually commence as a minute nodule, which may gradually increase until it projects as a large fungating tumour from the orbit. They are not encapsuled, and although they may occasionally infiltrate the tissues in which they lie and cause secondary growths

FIG. 45.



Sarcomatous Tumours from the Brain.—*a.* A glioma of cerebellum. This represents the appearance ordinarily presented by these growths. *b.* A comparatively rare form of sarcoma, which consists of large nucleated cells enclosed within the meshes of a vascular network. The development of this tumour took place in the brain subsequently to that of spindle-celled growths —primarily in the thigh, and secondarily in the lung. × 200.

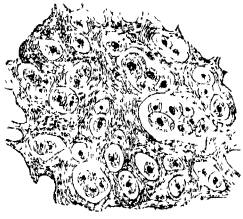
in their immediate vicinity, they very rarely reproduce themselves in the lymphatic glands or in internal organs. They are liable to small hæmorrhages into their structure, and sometimes become more or less caseous.

LYMPHO-SARCOMA.—This is a round-celled sarcoma, in which the matrix has developed into a more or less perfect reticulum, like that of lymphoid tissue. It may begin in lymphatic glands, or in connective tissue elsewhere. It is distinguished from lymphoma by its more rapid course, and by the formation of secondary growths by embolism.

ALVEOLAR SARCOMA.—This is a rare form of round-celled sarcoma, which was first described by Billroth. The cells, which are large, sharply defined, round or oval in

shape, and enclose prominent round nuclei, are separated from each other by a more or less marked fibrous stroma. In some parts this stroma forms small alveoli within which the cells are grouped; but careful examination will always show that in most parts of the section the stroma really penetrates between the individual cells. It is this last-named character which serves to distinguish these tumours from the cancers, with which, in many cases, they may easily be confounded. The accompanying drawing, made from a preparation kindly lent to me by Mr. R. J. Godlee, shows well their microscopical characters. (Fig. 46.) The stroma is often much more delicate; and the cell-masses are more rarely much larger than in the drawing. The cells are in close connection with the stroma. Vessels never pass in among them. Ziegler says the alveolar structure is due to transformation of intervascular tissue into cells whilst the vessels with some connective tissue remain as septa.

FIG. 46.



Alveolar Sarcoma.—From a tumour of the skin. × 200.

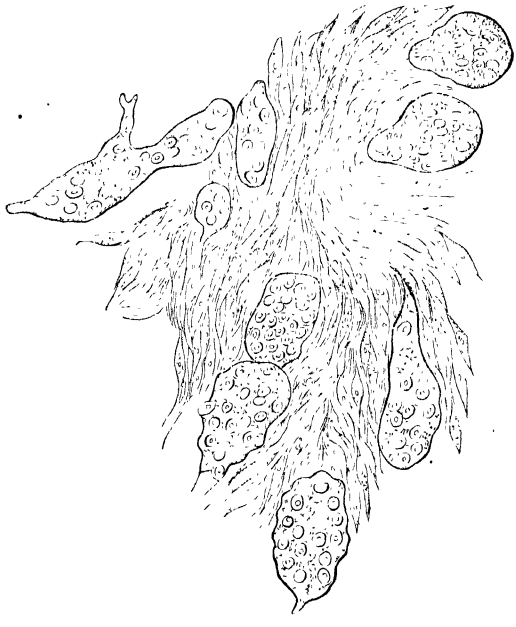
Alveolar sarcomata are met with principally in the skin, bones, and muscles. In the skin, where they are often multiple, they lead to ulceration. They tend to recur locally, and also to reproduce themselves in internal organs.

MYELOID SARCOMA.

This, which is the well-known **myeloid** tumour, is somewhat allied to the spindle-celled growths. It possesses, however, certain histological peculiarities which probably depend upon the characters of the tissue from which it grows. Myeloid tumours nearly always occur in connection with bone, and most frequently originate in the

medullary cavity. They consist of the large, many nucleated cells already described as "myeloid cells,"—which resemble the cells of the medulla in a state of excessive nutritive activity—together with numerous fusiform cells like those met with in the spindle-celled varieties. There

FIG. 47.



Myeloid Sarcoma. (Virchow.)

are also some smaller round and oval elements. The large myeloid cells which give to these tumours their distinctive characters, are usually much more numerous in those growths which originate in the medullary cavity than in those which spring from the periosteum. These

various forms of cells are almost in contact, there being very little intercellular substance. (Fig. 47.) The growths are sometimes very vascular, so much as to give rise to distinct pulsation. They often contain cysts.

Myeloid tumours almost always grow in connection with bone, the heads of the long bones being their favourite seat. They are also frequently met with springing from the periosteum of the upper and lower alveolar processes, where they constitute one form of **epulis**. When originating within the medullary cavity, the compact tissue of the bone becomes expanded over them, and they thus often communicate on palpation the peculiar sensation known to surgeons as "egg-shell crackling." These tumours are for the most part of firmer consistence than the other varieties of sarcoma; many of them are firm and fleshy, although others are softer, more resembling size-gelatin. They are not pulpy and grumous like the soft sarcomata, neither do they present the fasciculated appearance of the spindle-celled varieties. Their cut surface has a uniform succulent appearance, often mottled with patches of red. This red-brown or maroon colour (Paget) varies with the number of giant-cells present, and is very characteristic. They are often encapsuled by the periosteal covering of the bone from which they grow. They are rare after middle life, and are the least malignant of all the sarcomata.

BLOOD-CYSTS.

Tumours are occasionally met with into which so much hæmorrhage has taken place as to mask their real nature, and to give to them the appearance of blood-cysts. The nature of these blood-cysts has only recently been understood. They are now known to be in the majority of cases soft, round-, or spindle-celled sarcomata. They consist of broken-down blood-coagula, surrounded by an ill-defined layer of soft sarcoma-tissue. The microscope will also usually reveal sarcomatous elements amongst the altered

blood. These growths are exceedingly malignant, and hence the recognition of their sarcomatous origin is all-important.

CLINICAL CHARACTERS OF THE SARCOMATA.

The sarcomata occur most frequently in early and middle life, and, next to the carcinomata, are the most malignant of the new formations. They are especially characterised by their great tendency to extend locally and to infiltrate the surrounding structures, so that they are exceedingly prone to recur *in loco* after removal. Butlin has shown that sarcomata of certain parts almost always affect lymphatic glands, and early—namely, those of the testis, tonsil, lymphatic glands, and some fasciæ. Those of certain other parts never do; so that, on the whole, sarcomas present a contrast to cancers in this respect. They are also very liable to become generally disseminated, although this is not usual in the earlier stages of the disease. The secondary growths occur most frequently in the lungs. The dissemination is effected by means of the blood, and is owing to the thinness of the walls of their bloodvessels and to the immediate contact of these with the cells of the growth—conditions most favourable to the entrance of the cellular elements into the circulation. The dissemination of the sarcomata is, on this account, sometimes more rapid than that of the carcinomata. In the latter, extension in the early stage takes place principally by the lymphatics, and dissemination by the blood occurs only later in the disease. The secondary sarcomata usually resemble the primary one, but in exceptional cases the several varieties may replace one another.

These malignant properties, as has been seen, are possessed by the different varieties of sarcoma in very different degrees. As a rule, the softer and more vascular the tumour, and the less its tendency to form a fully developed tissue, the greater is its malignancy. The soft, round-celled, and large spindle-celled varieties are thus usually much more malignant than the firmer, small spindle-celled

growths. Their infiltrating powers are much greater, they sometimes infect the lymphatic glands, and tend to reproduce themselves very rapidly in internal organs. Many of the small spindle-celled tumours, after removal, never recur; whilst others recur locally several times, and ultimately reproduce themselves in distant parts. As a rule, largeness of the spindle elements and the existence in many of them of more than one nucleus, is an evidence of special malignancy. Central sarcomata of bone are much less malignant than subperiosteal; the latter, with sarcomata of the tonsil and testis, and melanotic sarcoma of skin, being among the most malignant of tumours. The presence of a capsule limiting the growth must also be taken into account in judging of the degree of its malignancy. It must, however, be borne in mind that even in a growth distinctly encapsuled, the sarcomatous elements may invade the adjacent structures. The myeloid growths are the least malignant; they may in exceptional cases give rise to secondary growths in internal organs, but "complete" removal gives a very good chance of non-recurrence. This sometimes occurs with growths having every appearance of malignancy.

CHAPTER XIX.

THE MYOMATA, NEUROMATA, AND ANGIOMATA.

THE MYOMATA.

THE Myomata are tumours consisting of muscular tissue. A new formation of muscle has been already described as being frequently associated with the ordinary process of hypertrophy, both of striated and of non-striated muscle—hyperplasia of the elements of the

muscle accompanying the increase in their size. (See p. 112.)

STRUCTURE.—The myomata consist either of striated or of non-striated muscle. The striated are exceedingly rare, only two or three examples having been recorded, and these were congenital. Striated cells, generally with non-striated, occur in sarcomata of the kidney and testis found in young children.

The myomata of **non-striated** muscle consist, like the physiological tissue, of elongated spindle-cells with rod-shaped nuclei, more or less isolated or grouped into fasciculi of various sizes, with a varying quantity of connective-tissue. The muscular elements either present a more or less regular arrangement, or pass in all directions through the tumour. The bloodvessels, which are usually not numerous, are distributed in the connective-tissue.

DEVELOPMENT.—Striated muscle-cells in congenital growths of organs developed from the Wolffian body are probably due to its inclusion in this body of cells from the adjacent muscle-plates. The much more common non-striated growths probably always originate from muscle. These may form distinctly circumscribed tumours surrounded by a fibrous capsule, or constitute ill-defined irregular masses in the midst of the muscular tissue in which they grow.

SECONDARY CHANGES.—Of these, the most frequent is calcification. Hæmorrhage, mucoid softening, and the formation of cysts, are occasionally met with; also ulceration and necrosis.

SEATS, &c.—Non-striated myomata are most frequently met with in the uterus. They occur also in the prostate, the œsophagus, and the stomach and intestines. They frequently become pedunculated and form polypi.

Myoma of Uterus.—The uterus is by far the most frequent seat of myomata, and here they constitute the so-called "uterine fibroid." In most of these muscular tumours of the uterus there is a large proportion of con-

nective tissue—hence the terms "fibroid" and "fibro-myoma." This is the case especially in older growths. Those newly developed, however, consist almost entirely of true muscular tissue. They either form firm hard masses, embedded in the uterine walls, or project into the uterine or abdominal cavities. When projecting into the uterus they constitute a common form of uterine polypus. They do not form till after puberty, and are commonest in elderly sterile females. Their growth is usually slow. Pregnancy causes them to enlarge rapidly, and they undergo some involution after delivery. These tumours are often multiple. The older ones are liable to become calcified. They also sometimes undergo mucoid softening, which gives rise to the formation of cysts in the tumour.

CLINICAL CHARACTERS.—Clinically, the myomata are perfectly innocent.

THE NEUROMATA.

The Neuromata are tumours consisting almost entirely of nerve-tissue. The term "neuroma" has been applied to many growths found in connection with nerves; fibrous, myxomatous, and gummy tumours growing within the nerve-sheath have been included under this head. True neuroma, however, is rarely met with, and is among the least frequent of all the new formations.

STRUCTURE.—The neuromata most commonly consist of ordinary medullated nerve fibres; they therefore resemble in structure the cerebro-spinal nerves, from which they most frequently grow. The nerve-fibres are associated with more or less connective-tissue. Virchow has described as exceedingly rare formations, also tumours composed of non-medullated fibres, and of ganglionic nerve-tissue.

DEVELOPMENT AND SEATS.—The neuromata always originate from pre-existing nerve-tissue,—either from the cranial or from the spinal nerves. Their growth is slow, they rarely attain a large size, but usually exist as

small single nodules. The bulbous ends of nerves in stumps are by some called **amputation-neuromata.** They often consist only of fibrous tissue, but may contain rolled-up nerve-fibres—attempts at regeneration rather than a tumour. They are usually intimately connected with the cicatricial tissue of the stump. Small tumours, single or multiple, may occur on any nerves, generally superficial ones. The majority of them are fibromata or myxomata; but some contain nerve-fibres.

CLINICAL CHARACTERS.—Clinically, the neuromata are perfectly innocent tumours. They often cause considerable pain.

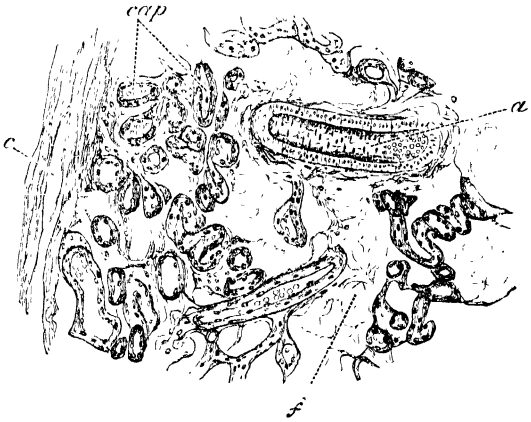
THE ANGIOMATA.

The Angiomata, or vascular tumours, consist of blood-vessels held together by a small amount of connective-tissue. They include the various forms of nævi, and aneurism by anastomosis. They may be divided into two classes—the **simple** or **capillary** angiomata, in which the new vessels resemble chiefly normal capillaries; and the **cavernous** or **venous** angiomata, in which the blood circulates in a cavernous structure similar to that of the corpus cavernosum penis. The characters of both are well shown in the accompanying drawings, made from specimens kindly lent by Mr. Boyd.

SIMPLE ANGIOMATA.—These consist of tortuous and dilated capillary vessels, held together by a small quantity of connective and adipose tissue. (Fig. 48.) It is doubtful what proportion of the vessels is due to dilatation of the original capillaries; but Ziegler thinks that many are formed this way. Some are of new formation. Very irregular dilatations are common. The capillary walls may be thin or thick, consisting of a double tier of cells. One or two supplying arteries can be seen in most sections. These growths generally occupy the superficial layers of the cutis, and form the port-wine stains and mother's marks; they are slightly or not at all elevated. Others lie in the subcutaneous or submucous

tissue, and may form large tumours. Their colour is red violet, or purple, according to the depth of the vessels and the rate of flow through them; the most frequent colour is red when superficial, bluish when subcutaneous. They are probably always congenital, though they may not be noticed for a few weeks after birth.

FIG. 48.



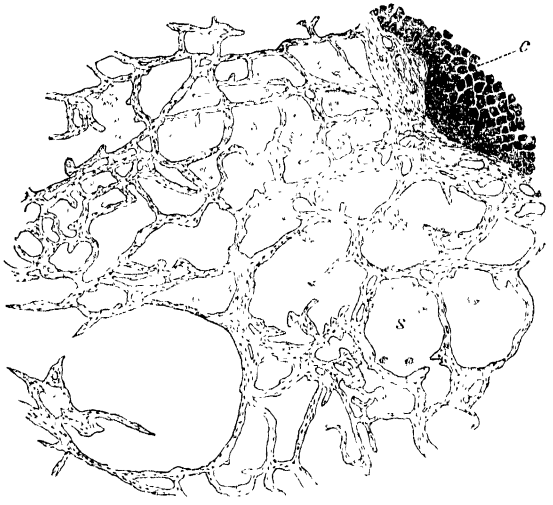
Capillary Nævus from Subcutaneous Tissue of a Child.—Cap. Vessels of new growth; *a.* normal artery; *f.* fat-cells; *c.* capsule. × 200, reduced ½.

Simple angioma is often combined with lipoma, glioma, sarcoma. Sometimes cysts containing dark fluid form

CAVERNOUS ANGIOMATA.—These are the venous vascular tumours. The growth is made up of irregular fibrous alveoli, which communicate freely with one another, and are lined with an endothelium similar to that of the veins (Fig. 49). These spaces are distended with blood, which is supplied to them by numerous tortuous vessels, and circulates with varying degrees of rapidity. The arteries open directly into the spaces. These growths are commonly of a bluish colour. They may be diffuse,

or form distinctly circumscribed tumours. They sometimes exhibit distinct pulsation. Their favourite seat is the skin and subcutaneous tissue. They may occur also in the orbit, muscle, liver, spleen, and kidneys. They may develop by dilatation of the vessels of a simple angioma. They may be congenital; but in the liver Ziegler thinks they develop after middle age, when the cells begin to atrophy.

FIG. 49.



Cavernous Nævus of Liver.—From a woman aged 39. *ss.* Large spaces bounded by fibrous walls, some containing blood *débris*; *c.* liver-cells (too large) toward which the growth is bounded by thick fibrous walls. × 40, reduced $\frac{1}{3}$.

ANEURISM BY ANASTOMOSIS.—The arteries of an area, especially on the head, become dilated, greatly elongated, and tortuous; perhaps new vessels form. Some are congenital, others follow injuries.

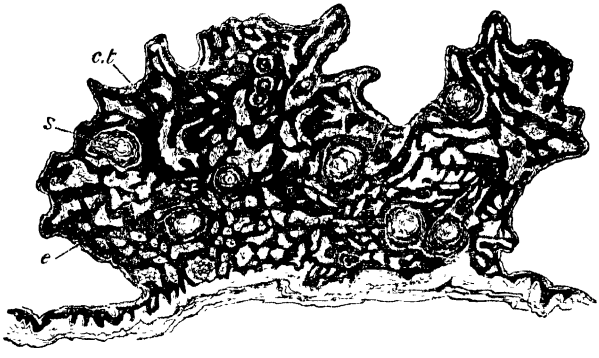
CHAPTER XX.

THE PAPILLOMATA.

THE Papillomata are new formations resembling in structure ordinary papillæ, and like these they grow from cutaneous, mucous, or serous surfaces, and from the interior of cysts. As all new growths on free surfaces tend to become papillary, it is probably the result of physical conditions. A wart would then be a fibroma become papillary by an accident of position.

STRUCTURE.—They consist of a basis of often richly cellular connective-tissue, which sends towards the

FIG. 50.



Section of Wart on Skin of Abdomen.—*e.* Epithelium; *c.t.* connective tissue continuous with epidermis and cutis; *s.* accumulations of horny epidermis deep down between the papillæ, looking in section like large nests. × 10.

surface numerous papillary processes, each supporting bloodvessels which end in a capillary network or single loop, the whole being enveloped in a covering of epithelium.

(Fig. 50.) The epithelial covering varies in character in different growths. In those of the skin, it is often very abundant, and the superficial layers are hard and stratified, forming a dense firm covering. In those originating from mucous surfaces, the epithelium forms a thinner investment, and is of a much softer consistence; whilst in those growing from serous membranes it often constitutes only a single layer.

The growth may be simple—consisting merely of enlarged papillæ, as in a common wart; or it may be complex, the papillæ being very numerous, long, and branched, giving off secondary and tertiary offsets. If the investing epithelium be very abundant, it may so enclose the whole mass as to give to it a more or less regular outline. More commonly, however, this is not the case; and, the epithelium not being sufficient to fill up the spaces between the papillæ, the growth presents a branched, villous, or cauliflower appearance. The blood-vessels are often very numerous, and are sometimes dilated and tortuous.

DEVELOPMENT.—The papillomata always originate from the skin, from mucous, or from serous membranes. As already stated, they owe their origin usually to some irritation, and must be regarded as occupying an intermediate position between inflammatory growths and tumours. They most frequently grow from pre-existing papillæ; sometimes, however, they occur where no papillæ exist, springing directly from the sub-epithelial connective tissue:—this is the case in the stomach and larynx. Their growth is usually slow. The individual tumours rarely attain a very large size, the larger forms being for the most part constituted of several smaller growths.

SECONDARY CHANGES.—Of these, ulceration and hæmorrhage are the most frequent. They occur especially in those growths which originate from mucous surfaces. The hæmorrhage is often very abundant, and may even endanger life. This is not unfrequently the case in the papillary growths of the bladder and intestine.

VARIETIES.—The varieties of papillary tumours depend principally upon their seat. Those growing from the skin include **warts** and **horny growths**. Warts are firm, have a dense epithelial covering, and are less prone to ulceration and hæmorrhage than those growing upon other parts. Horny growths appear usually to originate in the sebaceous follicles, by a continuous proliferation of their epithelium. The epithelium, together with the sebaceous secretion, forms a projecting horn, which increases by growth at its base. Such formations hardly come within the definition of papilloma. Larger and more vascular papillary tumours may, however, occur on cutaneous surfaces—such are the **condylomata** and **venereal warts** met with around the anus and upon the external male and female genital organs, as the result of irritating secretions.

The papillomata of mucous membranes are softer and more vascular than the preceding, they have a less dense epithelial covering, and are more prone to ulceration and hæmorrhage. Many of them come within the category of mucous polypi. They are met with on the tongue, in the larynx and nose, on the gastro-intestinal mucous membrane, on the cervix uteri, and in the bladder. In the bladder (villous tumour) and intestine they are often exceedingly vascular, and give rise to profuse hæmorrhage. Here they are not unfrequently confounded with villous epithelioma.

Papillomata of serous membranes never form distinct tumours. They are met with most frequently as small outgrowths from the synovial membrane in chronic diseases of joints.

CLINICAL CHARACTERS.—Clinically, the papillomata are innocent growths. They may, however, prove fatal from continuous ulceration and hæmorrhage: this is especially the case, as already mentioned, in papillomata of the bladder and intestine. In these situations they are easily mistaken for epithelioma; the symptoms of both are very similar, and it is often only after death that they

can be distinguished. In the case of the bladder a papilla may often be found in the urine, or removed in the eye of a catheter. In the papillomata the epithelium is **homologous**, being situated only *upon the surface* of the papillæ, and in no case growing *within* their connective-tissue basis. In the epitheliomata, on the other hand, it is **heterologous**, and it is met with at the base of the tumour in the subjacent connective tissue. (See Fig. 64.) It is important to remember that a growth which is primarily a simple papilloma may subsequently become an epithelioma. (See "Epithelioma.")

CHAPTER XXI.

THE ADENOMATA.

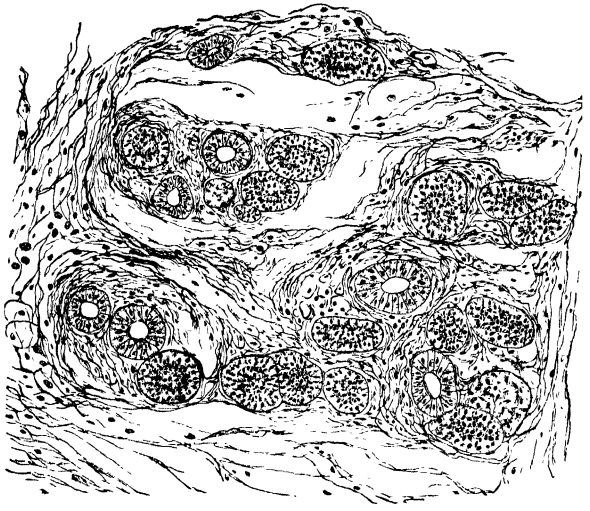
THE Adenomata—or, as they are more commonly called, **glandular tumours**—are new formations of gland-tissue, more or less atypical in structure, having an abnormal relation to the tissue around it, and incapable of performing the function of the gland they imitate. Their ducts do not enter those of the gland whence they spring.

STRUCTURE.—In structure the adenomata resemble the racemose or tubular glands.

The **racemose adenomata** consist of numerous saccules or acini, lined with small epithelial cells, which are often two or three layers deep. The acini communicate with each other, and are grouped together, being separated merely by connective tissue, in which are contained the blood-vessels. The connective tissue varies in amount; when much in excess of the normal the growth is called an **adeno-fibroma**. It may resemble the normal tissue, or, if growing rapidly, it will be much more richly cellular, containing round and spindle

elements; absolute anatomical distinction between such growths and sarcomata is impossible. The structure of these tumours is well shown in the accompanying drawing, made from a specimen kindly lent to me by Mr. Cantlie. (Fig. 51.)

FIG. 51.



Adenoma of Mamma. × 200, reduced ½.

All growths originating in glandular organs may be associated with more or less glandular structure. In the mamma, for example, sarcoma, myxoma, and other forms of tumour, are often so intermingled with the gland-tissue of the organ that it becomes difficult to say which is the predominant structure. In many cases it is evident that the development of such tumours is accompanied by an increase of the gland-tissue amongst which they grow. Thus are produced mixed forms—**adeno-sarcoma, adeno-**

myxoma, &c. These are not adenomata because the stroma is not that of normal gland.

The **tubular adenomata** grow from mucous membranes, and consist of groups of tubules lined with epithelium. They will be again alluded to hereafter.

DEVELOPMENT.—The adenomata almost always originate from pre-existing gland-structures. They generally grow slowly, and probably from some hitherto quiescent congenitally misplaced rudiment; otherwise it is difficult to explain the complete encapsulation and separation from the normal gland which distinguish adenoma from localised hypertrophy. The latter swelling remains in intimate relation with the gland, and is probably often of inflammatory origin.

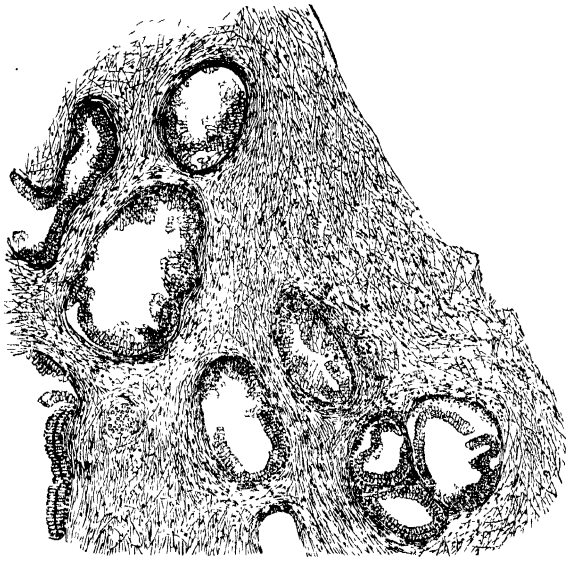
SECONDARY CHANGES.—The most frequent of these is fatty degeneration of the epithelium, which may give rise to the formation of small caseous masses in the growth. Dilatation of the saccules and tubules into cysts, and mucoid softening, are also common. The origin of cancer has several times been traced to an adenoma.

VARIETIES.—The word adenoma has been loosely used, as above pointed out, so as to include all new formations of gland-tissue. It is described as occurring in the following organs:—

Mamma.—This is much the most common seat of adenoma, or rather of adeno-fibroma; for a glandular tumour which is structurally indistinguishable from normal breast is very rare (Fig. 51). The arrangement of the epithelium, the number and size of the spaces, the proportion of stroma, and the number of cells it contains, is more or less abnormal (Fig. 52), hence the second name is generally most applicable. These tumours are called also "Chronic Mammary" and "Adenoid." They are encapsuled; round, oval, or lobulated; lying in or on the breast. They are of hard elastic consistence; their section is convex rather than cupped, of fibrous appearance, often lobulated, or showing a racemose structure even to the naked eye. These tumours are most common

in early life. They may be multiple. Many adeno-fibromata contain cysts, which may be very numerous, and vary in size from slight dilatations of ducts and acini up to cavities holding some ounces. They contain yellow, mucoid fluid, which may be reddish or brown from extravasated blood. Many are lined with cylindrical

FIG. 52.



Adeno-Fibroma of Mamma.—Showing new growth of gland structure and of connective tissue. × 100, reduced ½.

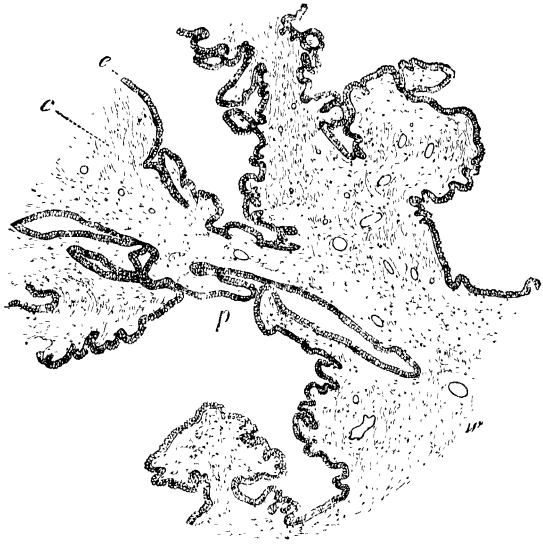
epithelium like that of the gland spaces; but others appear to be formed by localised softenings of the stroma. At first they appear on section like irregular and branched fissures, then like spaces full of fluid; but in other cases these are almost completely filled by papil-

lary fibrous growths covered by cubical epithelium, which grow in from their wall. These cystic growths are called **cystic adenoma**; or, if the stroma is richly cellular, **cystic adeno-sarcoma.**

The non-cystic growths must be distinguished from local and general hypertrophies of the gland.

Ovary.—Many compound ovarian cysts are really cystic tubular adenomata, and often contain papillary growths. (Fig. 53.)

FIG. 53.



Papillary Growth inside an Ovarian Cyst, projecting from its wall (*w*). They consist of loose connective-tissue (*c*), containing many branched cells, covered by a layer of columnar cells (*e*). Secondary processes are numerous (*p*). × 40, reduced ½.

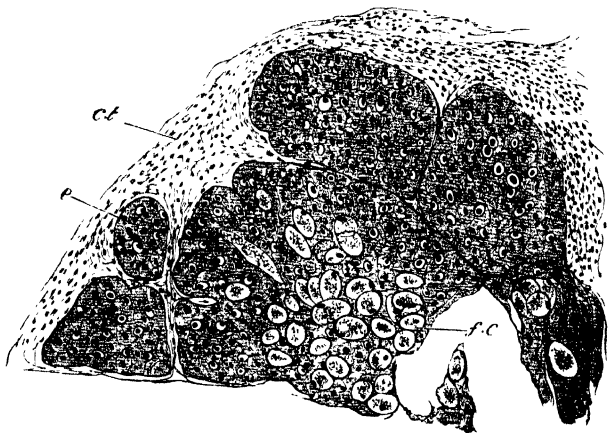
Testis.—No pure adenomata, but mixed tumours, like those in the parotid, occur.

Prostate.—Some of the tumours which form in this body in advanced age contain glands as well as muscle and connective tissue (Adeno-myoma).

Thyroid.—Apart from the hypertrophy of endemic goître and Graves' disease, distinct tumours having the structure of the thyroid occur in its substance.

Parotid.—Pure glandular tumours are infrequent, and the gland-epithelium is generally very atypical. Fibro-adenomata are commoner; but the ordinary "parotid tumour" is "mixed," containing cartilage, mucous tissue, &c. The other salivary glands are much more rarely affected.

FIG. 54.



Lobule of a Sebaceous Adenoma.—*c.t.* Connective tissue containing many cells, and forming capsule and septa. *e.* Saccule full of epithelial cells, few of which show signs of fatty degeneration—a clear space, pushing nucleus aside. In larger saccules degeneration is more general and extreme (*f.c*). × 200.

Liver.—Small encapsuled tumours having the structure of the liver are rarely found.

Glands of Mucous Membranes.—Racemose glands —mucous, Brunner's—may hypertrophy like the above. Gland-tissue enters largely into the structure of some of the "mucous" polypi which spring from every mucous membrane, especially in catarrhal states. In some cases the glands probably enlarge primarily; project, and become polypoid. In other cases it is thought that localised increase of connective tissue from inflammation may necessitate increase of the epithelial structures in relation with it. Polypi of the nose, stomach, intestines, rectum, and uterus are examples. The connective tissue is soft and œdematous; the surface is covered by the epithelium of the part.

Sebaceous and Sweat Glands.—"Adenomata" of these are hyperplasia rather than tumours; being uniform enlargements of the glands. Fig. 54, from a specimen of Mr. Boyd's, shows a small portion of a sebaceous "adenoma" from the chin of a child.

Calcification of the epithelial masses may occur, and Malherbe has shown that ossification of the fibrous stroma may also take place; such tumours are rare, and have been called osteomata of the skin.

Adenomata afford further support to Cohnheim's view concerning the nature of malignancy (p. 130). Almost invariably an adenoma or adeno-fibroma proves perfectly innocent. But now and again cases occur which appear clinically and microscopically to be ordinary adenomata, but which recur locally after removal. It is no explanation to call these sarcomata. Again, there are several cases on record of generalisation of tumours having the structure of normal thyroid: also some of ovarian adenoma.

The lumina of racemose adenomata are sometimes filled up with epithelial cells; it is then impossible to distinguish them microscopically from scirrhus in its earliest stage—that of multiplication of epithelium. Indeed, the origin of cancer from adenomata has several times been proved microscopically and clinically.

As sarcoma-tissue passes insensibly into fibrous, it is often impossible to say with certainty which name should be applied to the stroma of a tumour containing gland-tissue.

CHAPTER XXII.

THE CARCINOMATA.

THE Carcinomata or Cancers are most atypical new formations of cells of the epithelial type, grouped irregularly in the alveoli of a more or less dense fibroid stroma. The "epithelial type" implies origin from epi- or hypoblast, and the absence of intercellular substance; it does not imply any specific form of cell.

The alveolar structure, seen on section, has caused it to be said that cancer is an atypical gland-structure. Every tumour is atypical morphologically and physiologically; almost all are so structurally. But in cancer we have epithelial cells, often of the most abnormal form, filling up the lumina of gland-tubes (if it start from a gland), bursting through their basement or limiting membrane, and ramifying in the spaces of connective tissue. There is no type for such a process as this.

The cells vary markedly in character according as they spring from stratified epithelium, columnar epithelium, or the epithelium of acinous glands. They inherit, to a greater or less extent, the form and tendencies of the variety of epithelium from which they originate. Thus, cells of cancers springing from stratified epithelium tend also to undergo the ordinary epithelial evolution, ending in cornification; and in many cases they show prickle-cells. Columnar epithelium often retains its typical form, and continues to surround open spaces; but in other cases the cells multiply so as to fill the spaces, the

outermost cells generally retaining a cylindrical shape. Cells of acinous glands undergo no evolution; by multiplication they produce cells of their own kind, which may be much altered in shape by mutual pressure. Upon the retention by the cells of ancestral characters, the three chief varieties of cancer are based—the **squamous** and **cylindrical-celled epithelioma**, and **acinous cancer**. But ancestral peculiarities are not always retained. Certain cancers springing from stratified epithelium—perhaps from the small glands in relation with it—undergo no evolution, and are indistinguishable from scirrhus; and tumours springing from columnar epithelium are in many parts exactly similar to acinous cancer.

The name epithelioma was given to cancers springing from the epithelia, in opposition, as it was thought, to the cancers of connective-tissue origin. The distinction of the forms is of much less importance now that the epithelial origin of all is coming to be more and more recognised. (See "Development.")

Typical epitheliomata are so easily distinguishable by the above characters from acinous cancers that they are always described separately. We shall take the **acinous cancers** first.

STRUCTURE.—The definition shows that we have to describe, first, the epithelial cells; and, secondly, the stroma which forms the spaces in which they lie.

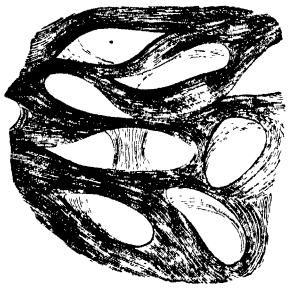
FIG. 55.

Cells from a Scirrhus of the Mamma. × 350.

The **cells** are characterised by their large size, by the diversity of their forms, and by the magnitude and prominence of their nuclei and nucleoli. (Fig. 55.) In size they vary from $\frac{1}{600}$ to $\frac{1}{1600}$ of an inch in diameter, the majority being about five times as large as a red blood-corpuscle. They are round, oval, fusiform, caudate, polygonal—exhibiting, in short, every diversity of outline.

These variations in form are principally owing to the mutual pressure to which, in their growth, they are subjected. The nuclei are large and prominent, round or oval in shape, and contain one or more bright nucleoli. The nuclei are, perhaps, most frequently single, but two are often met with, and in the softer and more rapidly growing cancers there may be more. The cells rapidly undergo retrogressive changes, hence they usually contain molecular fat. They are many of them exceedingly destructible, so that sometimes more free nuclei than cells are visible. Cells precisely similar to these are met with in other morbid growths, and also in the normal tissues. There is thus no *specific* "cancer-cell."

FIG 56.



The Alveolar Stroma from a Scirrhus of the Mamma.—The cells have been removed by pencilling. × 200.

The **stroma** varies considerably in amount, being much more abundant in some specimens than in others. It consists of a more or less distinctly fibrillated tissue arranged so as to form alveoli of various forms and sizes, within which the cells are grouped. (Figs. 56 and 58.) These alveoli communicate with one another, so as to form a continuous cavernous system. The characters of the stroma vary with the rapidity of its growth :—if this is rapid it will contain some round and spindle-shaped cells (see Figs. 60 and 65); if, on the other hand, it is slow, or has altogether ceased, the tissue will contain few or no cells, and will be denser and more fibrous in character. (Fig. 56.) The latter is the condition in which it is most commonly met with.

Within the stroma are contained the **blood-vessels.** These are often very numerous, and form a close network

round the alveoli. They are limited to the stroma, and never pass into the epithelial masses. This distribution of the blood-vessels is important, as distinguishing the carcinomata from the sarcomata, excepting some alveolar sarcomata, and tumours springing from endothelium.

In addition to the blood-vessels, the carcinomata possess also **lymphatics**. These, as has been shown by MM. Cornil and Ranvier, communicate freely with the alveoli. This explains the great tendency of cancer to infect the lymphatic glands. The characteristic cancer-juice consists of lymph containing cells scraped or pressed from the alveoli.

DEVELOPMENT.—The question of the genesis of carcinoma involves that of the genesis of epithelium generally. It is maintained by most histologists that epithelium can originate only from epithelium, and that the epiblast and hypoblast are the sources from which all epithelium is subsequently derived. Others admit that epithelium may originate also from connective tissue. A like difference of opinion exists as to the source of the epithelioid cells of cancer. By many—as Waldeyer, Thiersch, and Billroth — they are regarded as originating only from pre-existing epithelium. Others—amongst whom are Virchow, Lücke, Rindfleisch, and Klebs —maintain that they may be derived also from cells belonging to the connective tissue. It is also believed by some—as Köster—that many cancers originate from the endothelium of the lymphatics—*i.e.*, specialised connective-tissue corpuscles.

Nearly all modern observations tend to support the epithelial origin. This renders it impossible for true cancer to develop in any mesoblastic structure. Cases have been reported of primary cancer in lymphatic glands, in bone, in the membranes of the brain, &c. Here, either some small primary growth, which gave rise to no symptoms, has been overlooked, or some abnormality has existed, such as a detached piece of mamma lying near the axillary glands, or fœtal inclusion of an

epithelial rudiment; or the growth was one of those sarcomata which can be distinguished from true cancer only by the closest examination, or even by working out their development (alveolar sarcomata, cylindromata).

Epithelial cells are said to occur round a cancer, but quite isolated from it, lying in connective-tissue spaces. This isolation is very difficult to prove, and does not necessitate the origin of the cells from connective-tissue elements. For they may have been carried by the lymph-stream, aided by the spontaneous movements noted in cancer-cells by Carmalt. Often delicate chains of cells one to two inches long have been traced between a main growth and an apparently isolated nodule; such a chain might easily be interrupted. With better appliances, and more careful work, the reported cases of primary mesoblastic cancer are getting fewer and fewer.

It is most probable, therefore, that a cancer originates either in the growth of a resting embryonic epithelial rudiment (Cohnheim), or in the multiplication of some epithelial cells. Other conditions being favourable (see "Malignancy") the cells burst through any limiting or basement membrane, and grow in among the fibres of the connective tissue—naturally in the directions of least resistance—*i.e.*, often into lymph-spaces and channels. We then have epithelial cells lying actually in the lymph current, so glandular infection is easy to explain. Where resistance is great the growing cell-columns are narrow, where it is slight they widen out.

The connective-tissue bundles of the part at first alone form the **stroma**, but round-celled infiltration, the result of more or less intense inflammation excited by the epithelial invasion, soon appears. The round cells probably form fibroid tissue which contracts. At first, other elements of the part may persist in the stroma —*e.g.*, fat-cells in the breast, plain muscle-fibre in the prostate.

With this mode of growth, the carcinomata never become encapsuled, but gradually infiltrate surrounding

structures. This process of infiltration is very characteristic, and is more marked in cancer than in any of the malignant growths. A zone of small-celled infiltration is seen for some distance around the confines of the tumour, so that there is no line of demarcation between it and the normal structures. (See Fig. 57.)

SECONDARY CHANGES.—The most important of these is fatty degeneration. This always occurs to a greater or less extent in all the varieties of carcinoma. The more rapid the growth, the earlier does this retrogressive change take place, and the greater is its extent; hence it is usually most marked in encephaloid. It produces softening of the growth, which is often reduced to a pulpy cream-like consistence. Hæmorrhage, pigmentation, mucoid and colloid degeneration may also occur, with cyst-formation. Cysts may be due also to blocking of ducts—*e.g.*, in the mammæ. Calcification is very rarely met with. Formation of an abscess is rare, but important.

VARIETIES.—The most convenient classification, and that which is now generally adopted, divides the carcinomata into two chief groups:—**acinous cancer** and **epithelial cancer**; acinous cancer includes as varieties, **scirrhus** or **chronic** cancer; **encephaloid** or **acute** cancer; and **colloid** or **gelatiniform** cancer. Epithelial cancer includes **squamous** and **cylindrical-celled epithelioma.** This division is based principally upon the relative proportion of the stroma to, and upon the type of, the epithelial elements.

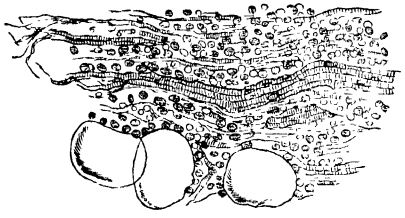
SCIRRHUS.

Scirrhus or **chronic** cancer is characterised by the large amount of its stroma and by the chronicity of its growth. The slow development of scirrhus probably accounts in great measure for the peculiarities in its structure and physical characters.

The epithelial growth, although at first it may be

luxuriant, quickly subsides. The elements soon atrophy and undergo retrogressive changes. They are most abundant in the external portions of the tumour, where growth is taking place; in the central portions they may be almost entirely wanting. The accompanying figures (Figs. 57

FIG. 57.

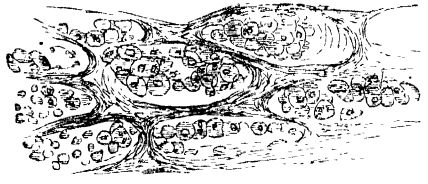


Scirrhus of the Mamma.—A thin section from the most external portion of the tumour, showing the small-celled infiltration ("indifferent tissue") of the muscular fibres and adipose tissue in the neighbourhood of the gland. × 200.

and 58) show the appearances presented by scirrhus of the mamma in the earlier stages of its development.

The degeneration of the epithelial elements is probably owing to the excessive growth of the stroma, and to the

FIG. 58.



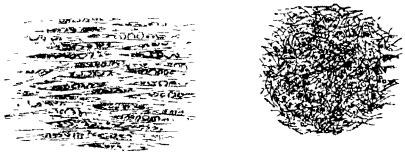
Scirrhus of the Mamma.—A portion of the tumour somewhat internal to that represented in Fig. 57, showing the characteristic alveolar structure of the cancer. × 200.

subsequent induration and contraction which it undergoes. It quickly assumes the characters of cicatricial tissue, and becomes hard and indurated. This causes obstruction

and obliteration of the blood-vessels which it contains, and it is probably to this interference with the vascular supply that the arrest in the development of the cancer is owing. The whole of the central portions of the growth may thus ultimately consist simply of dense fibroid tissue, amongst which are contained atrophied epithelial cells and fatty débris (Fig 59), the periphery being the only part where the epithelial structure is visible. The amount of atrophy and contraction varies considerably in different cases.

The physical characters of scirrhus are in the same way due to the abundance of its stroma. The growth is firm and hard, and is usually depressed in the centre, owing to the contraction of the fibroid tissue and atrophy of cells. This is very characteristic of scirrhus of the breast, where it causes retraction of the nipple and puckering of the superjacent structures. The growth is very hard, and

FIG. 59.



Scirrhus of the Mamma.—A section from the more central portions of the tumour, showing the atrophy of the epithelial cells, the diminution in the size of the alveoli, the fibroid tissue, and the fatty débris. *a.* earlier stage; *b.* more advanced. × 200.

creaks under the knife. The surface of the section is generally cupped, and of greyish-white, semi-translucent appearance ("like an unripe pear"), more or less mottled with dots and streaks of opaque yellow, due to fatty epithelium in alveoli or milk-ducts. The latter may be cystic. The central parts are pale and fibroid; the more external are pink, because contraction has not obliterated the vessels, and less firm than the central portions of the

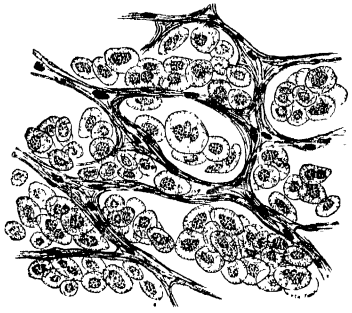
growth. They yield, on scraping, a juice which is rich in nucleated cells, free nuclei, and granules.

Scirrhus is most commonly met with in the female breast, and in the alimentary canal—especially in the œsophagus, pylorus, and rectum. It also occasionally occurs in the skin. The secondary growths to which it gives rise are often encephaloid.

ENCEPHALOID CANCER.

Encephaloid or **acute** cancer is very closely allied to the preceding, from which it differs merely in the greater rapidity of its growth, and the consequent small amount of its stroma, and the softness of its consistence. Encephaloid and scirrhus cannot be regarded as in any way constituting distinct varieties of carcinoma. There are all intermediate stages between them (scirrho-encephaloid);

FIG. 60.



Encephaloid Cancer.—From a secondary cancer of the liver, showing the large size of the alveoli and the thinness of their walls. In the latter, small cells are visible. The large epithelial cells are commencing to undergo fatty metamorphosis. × 200.

and their structural and clinical differences are accounted for by differences in rapidity of growth, which probably depends upon the vascularity of the part in which they are situated.

The epithelial growth in encephaloid is rapid and abundant; the cells, which may be either larger or smaller than those in scirrhus, quickly undergo fatty degenêration, so that often more free nuclei than cells are visible.

The proportion of stroma is very small, and, owing to the rapidity of its growth, it is much less fibrous than that of scirrhus, and does not undergo a similar cicatricial contraction. (Fig. 60.) The blood-vessels are often very abundant, and the tissue supporting them being soft and non-resistent, hæmorrhage occasionally takes place.

Encephaloid cancer is of a soft brain-like consistence, the central portions, where fatty degeneration is most advanced, often being completely diffluent. The tumour is sometimes more or less lobulated. On section, the undegenerate parts are grey, pinkish, soft and translucent, whilst the degenerate form a white pulpy mass, much resembling brain-substance, which is often irregularly stained with extravásated blood.

Encephaloid is much less common than scirrhus cancer. It is most frequently met with in internal organs as a **secondary** growth. It also sometimes occurs primarily in the testis and mamma. It may fungate and bleed (fungus hæmatodes). Many growths formerly described as encephaloid cancer are soft sarcomata. (See p. 163.)

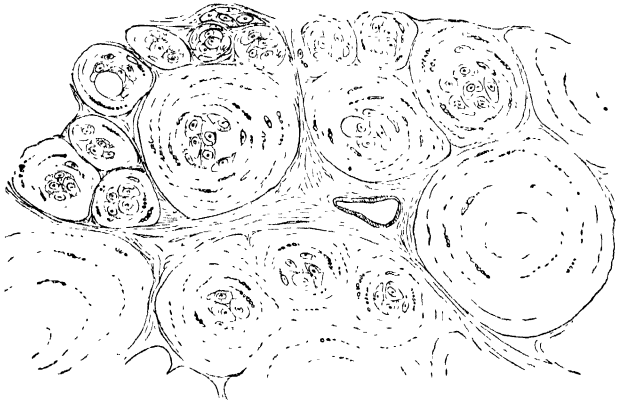
COLLOID CANCER.

Colloid, alveolar, or **gelatiniform** cancer, though sometimes regarded as a distinct variety of cancer, is simply one of the preceding forms which has undergone a mucoid or colloid change. The frequency with which non-cancerous growths which have undergone these forms of degeneration have been confounded with colloid cancer, has already been alluded to. (See "Colloid Degeneration.")

The alveolar structure in colloid cancers is very marked. The alveoli have very thin walls; they are large, distinct,

and more or less spherical in shape. This large size and distinctness of the alveoli is owing to their distension by products of degeneration. These form gelatinous colloid material, which is glistening, translucent, colourless, or yellowish, and of the consistence of thin mucilage or size-gelatin. In the main it is perfectly structureless; within it, however, are embedded a varying number of epithelial cells. (Fig. 61.) These cells present a peculiar appearance: they are large and spherical in shape, and are distended with drops

FIG. 61.



Colloid Cancer.—Showing the large alveoli, within which is contained the gelatinous colloid material. × 300. (Rindfleisch.)

of the same gelatinous material as that in which they are embedded. (See Fig. 61.) Many of them display a lamellar surface, their boundary being marked by concentric lines. It would appear that the colloid change commences in the cells, which become gradually destroyed in the process. In other cases the cells, with the exception of slight fatty metamorphosis, are but little

affected, and the substance distending the alveoli is more viscid and mucoid in character. This is due to a mucoid degeneration of the intercellular substance, rather than to a colloid change commencing in the cells. (See "Mucoid Degeneration.")

Colloid cancer is most frequently met with in the stomach, in the intestine, ovary, and in the peritoneum. In the latter case it is either secondary or the growth is a sarcoma.

EPITHELIOMA.

Epithelioma, or **epithelial cancer,** constitutes a much more distinct variety of carcinoma than either of the preceding; but transitional forms between it and scirrhus are occasionally met with. It differs from the other varieties of cancer in always growing in connection with a cutaneous or mucous surface—the junction of the two being a common seat—and in its epithelial elements closely resembling the squamous variety of epithelium.

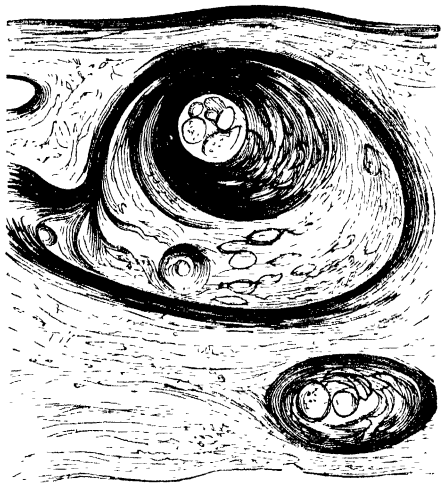
The cells of epithelioma are in the main indistinguishable from those met with on the cutaneous surfaces, and on the mucous membrane of the mouth. They vary in size from $\frac{1}{300}$ to $\frac{1}{1000}$th of an inch in diameter, the average being $\frac{1}{700}$th. They contain usually a single nucleus; frequently, however, the nuclei are multiple. (Fig. 62.) They are often considerably flattened and distorted in shape, owing to the pressure to which, in their growth, they are subjected, but they are not so multiform as in the other varieties of carcinoma; nor do they exhibit the

FIG. 62.

Cells from an Epithelioma of the Lip. × 250.

same marked tendency to fatty degeneration. The arrangement of the cells is peculiar: some of them are situated in irregular tubular-shaped lobules which communicate with each other; others are less regularly grouped in masses of various sizes amongst the meshes of a stroma. As the cells increase in number they tend to become arranged concentrically in groups, so as to

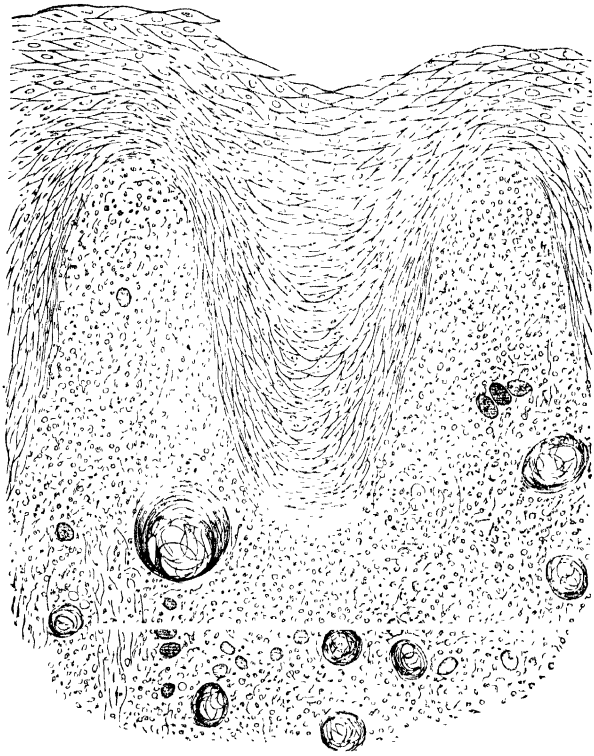
FIG. 63.



Epithelioma of the Lip.—Showing the concentric globes of epithelial cells. × 100.

form globular masses. These masses are the "**concentric globes,**" or "**epithelial nests,**" which are so commonly met with wherever squamous epithelium is undergoing rapid growth, and which, though not distinctive or essential, are exceedingly characteristic of epithelioma. As the epithelium multiplies, the peripheral layers of cells become flattened by pressure against the surround-

ing structures, whilst those in the centre remain more or less spherical in shape, like those in the deeper layers of



Epithelioma of the Tongue.—A thin vertical section, showing the excessive epithelial growth upon the surface of the papillæ, and the extension of the epithelial elements into the subjacent connective tissue. The sub-epithelial tissue is infiltrated with small ("indifferent") cells, amongst which are seen the epithelial elements both single and forming concentric globes. × 100.

the epidermis (Fig. 63.) The cells may be so closely packed as ultimately to become hard and dry like those of the nails and hair, and the globes are then of a brownish-yellow colour, and of a firm consistence. The globes are often large enough to be readily visible to the naked eye, and, owing to the onion-like arrangement of the epidermic scales, they usually present a fibrous appearance.

The stroma presents every variation between rapidly growing embryonic and an incompletely fibrillated tissue. It may be tolerably abundant, or almost entirely wanting. It rarely forms such a marked alveolar structure as that which characterises the other varieties of carcinoma, and usually consists simply of a small-celled infiltration surrounding the epithelial elements, which may ultimately become developed into a more or less completely fibrillated tissue. (Fig. 64.)

The development of epithelioma takes place by down-growth of the surface-epithelium of skin or certain mucous membranes into the connective tissue and deeper parts, just as is described on p. 190. Varieties which do not show epithelial evolution, especially the small-celled "rodent ulcer," are believed to arise from sebaceous glands and hair follicles. (Fig. 64.)

Epithelioma usually presents itself in the first place either as a small hard ulcer, as an indurated fissure, or as a subcutaneous induration or nodule, which subsequently ulcerates. The surface of the ulcer is irregular, and may be sloughy; often it is clean, and covered by large firm, bluish-red granulations, consisting largely of epithelium; more rarely the surface is markedly warty. The tumour itself is firm in consistence, often more or less friable, and on section presents a greyish-white granular surface, sometimes intersected with lines of fibrous tissue. The cut surface yields on pressure a small quantity of turbid liquid, and in many cases also a peculiar, thick, crumbling, curdy material can be expressed, which often comes out in a worm-like shape, like sebaceous matter from the glands of the skin. This latter is very characteristic. It

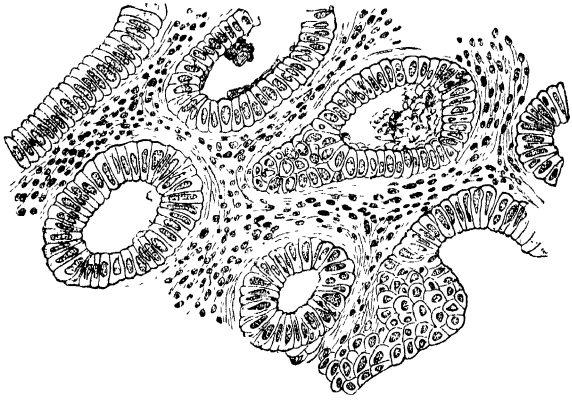
is composed of fatty epithelial scales, and on being mixed with water it does not diffuse like the juice of other cancers, but separates into minute visible particles. If it is very abundant, the cancer is soft and friable, and the material can be seen on the cut surface as small scattered opaque dots.

Irritation has more to do with the causation of epitheliomata than of other kinds of cancer. Some, as sweep's cancer of the scrotum from soot, and epithelioma of the arm of workers with tar or paraffin, appear to be due simply to irritation in people the physiological resistance of whose connective tissue is sufficiently diminished by the irritation or otherwise to permit invasion. Other epitheliomata occur at those spots at which, the process of development being complicated, errors are likely to occur; resulting, as Cohnheim supposes, in the formation of arresting, embryonic rudiment. Such spots are, the lower lip, tongue, ala nasi, eyelid, cervix uteri, gullet where crossed by bronchus, &c. (see p. 130). Many of these are points exposed to irritation. It usually infects the lymphatic glands, but rarely occurs in internal organs.

Cylindrical Epithelioma, or Adenoid Cancer.—These terms are applied to those forms of epithelial cancer which grow from mucous membranes with columnar (cylindrical) epithelium, as from those of the stomach and intestines, and especially the rectum and uterus. In these tumours the epithelial elements are similar to those of the mucous membrane from which they grow. They are cylindrical in shape, and are arranged perpendicularly to the walls of the alveoli in a manner precisely analogous to that of the columnar epithelium on the mucous surface. (Fig. 65.) The slower the growth, the more typical the gland formation; in rapid growths, and recurrences, the cells are small, the lumina imperfect. The latter may be filled up, and the growth be indistinguishable from glandular cancer, except by its edge. The growths are of a soft, and often gelatinous consistence; they tend strongly to undergo colloid degeneration. These tumours cause secondary

growths in the lymphatic glands, and sometimes in the liver, lungs, and bones, which possess the same characters as the primary cancer. The distinction between them and simple adenomata depends upon the invasion of tissue by the cancers.

FIG. 65.



Cylindrical Epithelioma.—From the colon. × 200, reduced ½.

CLINICAL CHARACTERS OF THE CARCINOMATA.—In speaking of the clinical characters of the cancers, it is important in the first place to make a distinction between epithelioma and the other varieties. Epithelioma, so far as its malignancy is concerned, occupies a very inferior position to scirrhus, encephaloid, and colloid. These latter varieties of carcinoma possess in the highest degree malignant properties. They extend locally, invading indiscriminately the tissues amongst which they grow, and reproduce themselves in the lymphatic glands and in internal organs. In the process of dissemination, however, they present some peculiarities which distinguish them from growths which are sometimes equally malignant—viz., the sarcomata. The carcinomata are charac-

terised by their great tendency to reproduce themselves in the neighbouring lymphatic glands. This implication of the lymphatics is usually much more marked than in the sarcomata, in which it occurs only in certain situations (p. 169), and is probably owing to the communication of the lymphatic vessels with the alveolar spaces of the cancerous growth. The general dissemination in internal organs, on the other hand, is often effected much less readily in carcinoma than in sarcoma, and the course of the former is therefore sometimes more protracted than that of the latter. This difference is explained by the difference in the distribution of the blood-vessels:—in carcinoma, these are contained in the stroma, and very rarely come into contact with the cells of the growth; whereas in the sarcomata, they ramify amongst the cells, and their walls being composed of thin embryonic tissue like that of the growth which they supply, dissemination through the medium of the blood is rapidly and readily effected. In carcinoma, the lymph being so important a medium of infection, the reproduction of the growths in internal organs may be considerably delayed. The progress of the disease becomes arrested by the lymphatic glands, and its further dissemination is often effected only after these have become very generally and extensively involved.

With regard to the difference in the clinical characters of these three varieties of carcinoma—the dissemination of encephaloid takes place much more rapidly than that of scirrhus, owing to the greater rapidity of its growth, its greater vascularity, and the greater activity of its epithelial elements. Colloid is somewhat inferior in the degree of its malignancy to both scirrhus and encephaloid.

Epithelioma is of all cancers much the least malignant. Its malignancy varies curiously with its seat; thus, on the skin of the face epithelioma has generally a very chronic course, and rarely affects even the glands; on the tongue, its course is often so rapid, affection of the glands so early, and cachexia and death so speedy, that it must

be ranked among the most fatal of tumours. It extends locally, and often infects the neighbouring lymphatics, but it comparatively rarely reproduces itself in internal organs. This is probably owing to the size and character of its epithelial elements, which render them much less liable to be transmitted by the blood and lymph-streams than are the cells of the other varieties of cancer.

In all the varieties of carcinoma there is a tendency for the secondary growths to repeat the peculiarities of the primary one. This is most marked in epithelioma. In scirrhus, the secondary growths in internal organs, although sometimes resembling the primary tumour, are often more rapidly developed, are softer and more vascular, and in accordance with the distinction which has been made between scirrhus and encephaloid, they must be regarded as belonging to the latter variety of cancer.

THE TERATOMATA.

These tumours can only be mentioned. They are congenital and occur chiefly in the sacral region (coccygeal tumours), the head and neck—points at which double monsters are united; but they may be internal. Many of them are due to the inclusion and imperfect development of one fœtus within another; others to abnormal development of the tissues of one fœtus. They are most complex, and may contain all the tissues of the body up to ganglion cells, more or less confusedly mixed. They may be very large at birth, or may not attract notice till later. Dermoid cysts belong to this group.

CHAPTER XXIII.

CYSTS.

In addition to the new growths already described, there is a large class of formations, many of which cannot be regarded as "tumours" in the strict application of this term. These are the **cysts,** or **cystic tumours.**

A **cyst** is a cavity containing liquid or pultaceous material, which is separated from the surrounding structures by a more or less distinct capsule. It may be a new formation, or a pre-existing structure which has become distended by its own secretion, or by extravasation into it. The former only comes within the category of new growths; but, for the sake of convenience, it will be advisable to consider them both under one head.

There are thus two principal modes by which cysts originate—one, the most frequent, by the gradual accumulation within the cavities of pre-existing structures, of substances which are, for the most part, products of their own formation—being in some cases a secretion, and in others a cell-growth; the other, by the independent formation of a cyst in the tissues.

The accumulation of secretions and of other products within pre-existing cavities, may be effected in the three following ways:—

1st. By the retention of the normal secretion owing to the closure of the excretory ducts—as so often occurs in sebaceous glands.

2nd. By excessive secretion, the cavity being unprovided with an excretory duct—as in the distension of bursæ.

3rd. By the extravasation of blood into the cavity—as in hæmatocele.

The independent formation of a cyst may take place:—

1st. By the softening and liquefaction of the tissues

in some particular part, owing to mucoid or fatty changes. The tissues around the softened matters become condensed, and ultimately form a kind of cyst-wall.

2nd. By the collection of fluid in certain spaces of connective tissue, and their subsequent enlargement and fusion. The surrounding tissue becomes condensed, and forms a cyst-wall; and this may in some cases become lined with flattened connective-tissue cells (endothelium).

3rd. By the formation of a cyst-wall around foreign bodies, parasites, or extravasated blood.

STRUCTURE.—The wall of the cyst will vary in its nature according as it is that of a pre-existing or a newly formed cavity. In the former case, it will possess an epithelial lining which will present the same characters as that of the gland, serous membrane, or other structure from which the cyst originated. If the cyst is of independent formation, there is no endothelial lining to the fibrous capsule; but one may develop later, as in false bursæ. The cyst-wall is sometimes firmly connected with the adjacent parts, so that it can only with difficulty be separated; in other cases the union is much less intimate. Instead of being a distinct structure, it may be simply the surrounding tissue which has become dense and fibrous in character.

The contents of cysts are very various, and may serve as a basis for their classification. In the retention-cysts, they will vary with the nature of the normal secretion—serum, sebaceous matter, saliva, milk, seminal fluid, and other substances are thus found in these cysts, more or less altered in character from being retained in a closed cavity. In the exudation-cysts, serum is the most frequent constituent; and in extravasation-cysts, blood. In those cysts which originate from the softening and breaking down of tissue, the contents are the products of retrogressive tissue-metamorphosis, and usually consist largely of mucin, fatty matters, and serum.

SECONDARY CHANGES.—These may take place in the wall of the cyst or in its contents. The cyst-wall

itself may become the seat of new growths, and produce secondary cysts, villous, glandular, and other structures:—this occurs in many compound ovarian cysts. It may also be the seat of an inflammatory process, which terminates in suppuration and granulation, and by this means the cyst frequently becomes obliterated, its contents being either absorbed or discharged externally, and the cavity closing by granulation. Calcification and ossification of the wall may also occur. The contents of cysts undergo various changes, owing to their retention in a closed cavity. The secretions become altered in character, thickened, and viscid. Epithelial elements undergo fatty changes, and so give rise to cholesterin crystals. Calcification of the contents is also common.

Cysts may be **simple** or **compound.** A simple cyst consists of a single loculus. A compound or multilocular cyst is one consisting of numerous loculi, which either communicate with one another or remain isolated. Another variety of compound cyst consists of a cyst with endogenous growths, the larger cyst having others growing in its walls. A compound cyst may become a simple one by the destruction of its walls.

Cysts are frequently associated with other growths, hence the terms—"cystic-sarcoma," "cystic-cancer," &c. It is especially in those growths which originate in glandular structures, as in the mamma, testicle, and ovary, that this combination is met with. The cystic development may almost entirely obliterate the structure of the tumour in which it takes place, so that ultimately the latter becomes converted into a combination of cysts. In other cases large papillary masses of the tumour grow into the cystic cavities. Considerable difficulty is thus not unfrequently caused in determining the nature of the original growth.

CLASSIFICATION.—Cysts may be most conveniently classified according to their mode of origin, thus:—

CLASSIFICATION OF CYSTS.

I. *Cysts formed by the accumulation of substances within the cavities of pre-existing structures.*

A. RETENTION CYSTS. — Cysts resulting from the retention of normal secretions. These include—

α. *Sebaceous Cysts.*—These are formed by the retention of secretions in the sebaceous glands.

β. *Mucous Cysts.*—These are formed by the retention of secretions in the glands of mucous membranes.

γ. *Cysts from the retention of secretions in other parts*, including—Ranula, when due to occlusion of the salivary ducts; Encysted Hydrocele, from occlusion of the tubuli testis; cysts in the mammary gland, from obstruction of the lacteal ducts; simple and some compound cysts of the ovary, from dilatation of the Graafian follicles; and simple cysts of the liver and kidneys.

B. EXUDATION CYSTS. — Cysts resulting from excessive secretion in cavities unprovided with an excretory duct. These include Bursæ, Ganglia, Hydroceles, Meningoceles, Cystic Bronchocele, and many cysts in the broad ligament.

C. EXTRAVASATION CYSTS. — Cysts resulting from extravasation into closed cavities. These include Hæmatocele, and some other forms of sanguineous cysts.

II. *Cysts of independent origin.*

A. CYSTS FROM SOFTENING OF TISSUES.—These are especially common in new formations, as in chondroma, lipoma, sarcoma, &c.

B. CYSTS FROM EXTRAVASATION INTO SOLID TISSUES —*e.g.*, brain, soft new-growths.

C. CYSTS FROM EXPANSION AND FUSION OF SPACES IN CONNECTIVE TISSUE.—These include—

a. Bursæ, originating from irritation and exudation into the tissues.

β. Serous cysts in the neck, hygroma (often congenital).

γ. Many compound ovarian cysts.

D. CYSTS FORMED AROUND FOREIGN BODIES, EXTRAVASATED BLOOD, AND PARASITES.

E. CONGENITAL CYSTS.—These include many Dermoid cysts. These appear often to be the remains of blighted ova. Their wall has more or less perfectly the structure of skin; they contain fatty matters, hair, teeth, bones, &c.

CHAPTER XXIV.

CHANGES IN THE BLOOD AND CIRCULATION.

THE vascular system is a closed system of tubes, capable of varying in capacity, and having inserted at one point a muscular organ, so constructed that it can receive on one side venous blood at a minus pressure, and send out on the other arterial blood with force sufficient to carry it right through the systemic or pulmonary circulation. The heart-force is aided by the pressure of contracting muscles upon valved veins, and by thoracic aspiration. Each time an artery branches, the sectional area of the arterial system is increased; so also is its extent of surface. But, in both these respects, by far the greatest increase takes place in the region of arterioles and capillaries. Increase of surface means increase of friction, and enlargement of the area upon which a given force has to act, must also diminish the effect of that force. Conse-

quently, the blood-stream becomes suddenly slowed in the arterioles and capillaries. The arterioles vary in diameter much more than do larger arteries, for they contain proportionately much more muscle. The resistance in the arterioles, therefore, varies enormously under diverse influences; but the diameters of capillaries seem to change only in reponse to variations in pressure. The sectional area of the venous system, on the other hand, diminishes from the capillaries to the heart, and the rate of flow increases proportionately as the region in which thoracic aspiration acts is approached.

Gravity must not be regarded as in any way a cause of circulation; what the blood loses or gains on its way from the heart will be exactly balanced during its return to the heart. But though gravity has nothing to do with the driving force, it increases the pressure in vessels. This is best shown by a U-tube:—the pressure varies directly as the height of the columns in the limbs, but no movement occurs unless a driving force is added.

The quantity of blood in the body may be regarded as constant in normal states.

Circulatory disturbances may be produced in many ways. The heart may act so feebly or be so damaged structurally (valve-disease), that too little blood enters the arteries at each stroke, and generally at a pressure less than normal. As a result the arterial supply of all parts is diminished, blood lags in the veins, and a less quantity than normal enters the heart during each diastole. More rarely, the heart may act so forcibly as to rupture delicate or diseased vessels.

Supposing the heart to act normally, it is obvious that, with a constant blood-mass, the total capacity of the vascular system must be kept within certain limits. It may easily dilate so as to contain all the blood (the abdominal veins alone would do this after section of the splanchnics), when the heart would receive none, and circulation would cease. Or, the arterioles may contract, so as to more or less completely stop circulation and drive all the blood into

the veins. Between these extremes there is a state of the vascular system, corresponding to any given heart-force, which is most favourable for the circulation: this is normal tonus. It is the province of the vaso-motor system to maintain this relation between heart and vessels. Enlargement of the vascular system, whether due to general or local diminution of vascular tonus, slows the circulation; diminution of the capacity of the system, in moderation, quickens it. In cases of local increase of tonus the blood which the more or less anæmic part should contain is thrown into the system at large, and raises the blood-pressure until the vaso-motor system causes other vessels to dilate compensatorily, so as to receive both their own blood and that of the contracted vascular area. Parts supplied by vessels so dilated are said to be in a state of "collateral hyperæmia." If, on the other hand, a vascular area dilates, the vaso-motor system generally causes other areæ to contract, so as to preserve the capacity of the vessels about the same, and thus keep up the pressure—that is to say, other parts become anæmic to provide the hyperæmic one with blood. This state might be called "collateral anæmia."

LOCAL ANÆMIA.

Local anæmia, or ischæmia, is diminution of blood in a part owing to diminished arterial supply. It may be partial or complete.

CAUSES.—The causes of diminished arterial supply to a part are all those conditions which either narrow or completely close the lumen of the supplying artery. The lumen of an artery may be diminished by disease of its walls—atheroma, calcification, or syphilitic thickening; or by pressure exercised upon it from without, as by new growths, stricturing scars, inflammatory exudations and mechanical effusions, especially in unyielding tissues, as

bones or tendon-sheaths. Complete closure of the vessel may result from some of the foregoing conditions, or, more commonly, from thrombosis, embolism, or ligature. In some cases the supply of blood is diminished by an increase in the natural resistance from irritation of the vaso-motor nerve. This occurs as the result of a low temperature, in some neuralgic and other nervous affections, and from the action of certain substances, such as ergot of rye, opium, &c. Anæmia may occur also from hyperæmia of other parts—*e.g.*, of the brain and skin, in congestion of the abdominal viscera; and from the presence of too little blood in the system, as after hæmorrhage, when the distal parts suffer most.

RESULTS.—A part with diminished arterial supply is usually paler, less tense, and of a lower temperature than natural. Its nutrition and function also are impaired, so that it may undergo fatty degeneration, atrophy, or die. These results were exemplified in the chapters on Atrophy, Fatty Degeneration, and Necrosis.

Obstruction of a large artery causes rise of pressure everywhere except in its own area; and this increased arterial pressure continues, endangering the safety of delicate or diseased vessels, until the extra blood thrown into the now curtailed arterial system is accommodated in some way. This is effected generally by compensatory dilatation of other vessels going to the anæmic part and anastomosing with branches of the obstructed vessel, partly by the increased arterial pressure which acts on all arteries alike, but chiefly by some obscure vaso-motor mechanism excited, probably, by the anæmia. These "collateral" vessels become larger, longer (tortuous) and thicker, until the circulation in the part has again become normal —*i.e.*, **collateral** circulation is established. At first probably all vessels having anastomoses with the obstructed one, dilate; but those which enlarge permanently are almost invariably branches on the same side as the obstruction—*e.g.*, *right* inferior thyroid and vertebral after ligature of *right* carotid. The primary anæmia, the blush and height-

ened temperature of vascular dilatation, and return to the normal, can be seen in limbs after ligature of main vessels.

In certain organs, however, there is either but one supplying artery, or others entering it are insignificant; further, in the spleen, kidneys, lungs, brain, and retina the branches of the main vessels communicate only by capillaries—such arteries are called **terminal** by Cohnheim. Here no collateral circulation can be established, and obstruction is necessarily followed by the gravest nutritive disturbance. The first effect of the plugging of such an artery is the stoppage of all supply through it; the arterioles empty themselves by contracting and pressure in them is reduced to *nil;* venous pressure, though low, is in excess of this, and blood regurgitates from the veins to fill the capillaries and arterioles beyond the stoppage—as may be seen with the microscope in a frog's tongue, of which one lingual artery has been tied. The arteries round about the area dilate, and their capillaries become full of blood; but even now the force of the stream in the latter is sufficient to overcome the resistance in only a few of the outlying capillaries of the obstructed area. Consequently we should find such an area dark from containing stagnant venous blood, but surrounded by a ring of arterial redness.

The changes which result from deprivation of arterial blood have been studied experimentally by Cohnheim. If the ear of a rabbit be ligatured at its root, and the ligature, after remaining on for from eight to ten hours, be removed and the blood again allowed to circulate, the organ becomes exceedingly vascular, red, swollen, and œdematous; and when examined microscopically the vessels are found to be dilated, and numerous white blood-corpuscles to have escaped from them into the surrounding tissue. The more prolonged the anæmia, the more abundant is the infiltration with leucocytes; and when the obstruction has lasted twenty-four hours small extravasations of red corpuscles also occur. If the ligature remain on for forty-eight hours the ear dies. From these observations

Cohnheim concludes—that when blood-vessels with their vasa vasorum are deprived of circulating blood for a sufficient length of time they lose their power of retaining the blood, and allow, first the liquor sanguinis and leucocytes, then red corpuscles, to escape from them, the escape taking place only through the capillaries and veins. The whole process can be watched in the tongue of a frog to the base of which a ligature has been applied. For the walls of blood-vessels to be thus altered, interference with the circulation must be very complete—a very little vascular supply serves to prevent the above phenomena; but imperfect nutrition is a step towards death, and must render tissues less resistant to injury—a wide-reaching fact, which must always be borne in mind. These observations explain all changes, from œdema to gangrene, which may follow ligature of the main artery of a limb, especially the femoral.

FIG. 66.

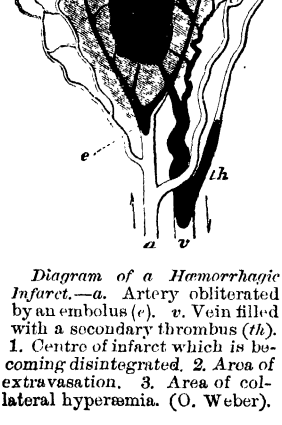


Diagram of a Hæmorrhagic Infarct.—a. Artery obliterated by an embolus (*e*). *v.* Vein filled with a secondary thrombus (*th*). 1. Centre of infarct which is becoming disintegrated. 2. Area of extravasation. 3. Area of collateral hyperæmia. (O. Weber).

To return to the blocked terminal artery. When circulation is arrested in its area and the vessels are choked with regurgitant venous blood, the above changes from mal-nutrition soon set in:—fluid, and then corpuscles, pass out into the tissues without any rupture of the vessel. The tissues become crammed with red corpuscles; and from the mode of distribution of the vessels (Fig. 66), the part thus affected is generally wedge-shaped on section, and the base of the wedge lies on the surface of the organ. The base is slightly raised above the general surface and surrounded by a ring of arterial

redness, whilst the section shows the **infarct** to have a black-red colour, like damson-cheese. (For later changes, see p. 247.)

By far the commonest cause of infarction is embolism (p. 241). A very important point is that all vessels do not resist equally the effects of anæmia—those of skin and muscle being most resistent; those of brain and intestine least. Strangulated gut is like a tied-off ear, but it dies much sooner. This power of resistance varies in individuals.*

* Litten ("Unters. ü. d. hämorrhag. Infarct, &c.:" *Deutsche Zeitschr. für Klin. Med.*, Band i. Heft 1) disputes the truth of Cohnheim's explanation of the whole process of infarction. The infarction of the kidney which follows ligature of the renal artery is not due to regurgitation from the renal vein, for it is even more intense when the renal vein also is tied. The kidney then swells greatly, becoming first congested, then infarcted. The congestion begins in the subcapsular zone of the cortex, and at the bases of the pyramids where the pelvis is attached, and it is due to the continued supply of the organ by small arteries (now much dilated) which spring from the lumbar, supra-renal and phrenic (Ludwig), and pierce the capsule, and to others from the spermatic which run up along the ureter. If the renal vein is left open, the kidney swells more slowly, because some of the blood entering from these arteries escapes by the vein; the stream is therefore away from, not towards, the kidney. But the most perfect proof that the infarction is due to supply through these arteries, and not to venous reflux is afforded by this experiment: the renal artery is rendered truly "terminal" by shelling the kidney out of its bed of fat, and the artery is then tied. Regurgitation should now occur from the open vein, but, as a rule, it fails to do so. A slight congestion of the organ sometimes occurs, but the gland remains much lighter and smaller than its fellow, of which the renal artery only has been tied, and never becomes the seat of hæmorrhage per diapedesin. It would seem, therefore, that in many cases the pressure in the renal vein is not sufficient to overcome the resistance of the capillaries and to produce an injection of them with blood, when the main artery and its small collaterals are tied; much less would it do so when the latter are pumping blood in beneath the elastic capsule, and thus increasing the intra-capsular pressure. If by coughing, vomiting, &c., the pressure in the renal vein is raised, infarction is more likely to occur; and it is produced in its severest form by clamping the vena cava inferior above the entry of the renal vein. These observations were extended with similar results to the spleen and lung.

When a truly "terminal" artery is blocked, no infarction occurs in the great majority of cases; its area remains pale and anæmic, and microscopic examination reveals no trace of red corpuscles. This

HYPERÆMIA.

Hyperæmia, or congestion, is excess of blood in the more or less dilated vessels of a part. It may be **active** or **arterial** and **mechanical** or **venous**. These two varieties must be considered separately.

ACTIVE OR ARTERIAL HYPERÆMIA.

Active hyperæmia is an excess of blood in the arteries of a part, with, in most cases, an acceleration of the flow.

CAUSES.—The immediate cause of active hyperæmia is in all cases **diminished arterial resistance.**

Diminished arterial resistance may be produced pathologically :—

1st. **By certain agencies which have a weakening or paralysing effect upon the involuntary muscle of vessel-walls.** Fatigue from previous prolonged contraction has this effect, as seen in the hyperæmia of the hands which follows snowballing. Warmth, too, is generally placed under this heading. Injuries of all kinds, when not acting suddenly and with extreme severity, produce a reflex hyperæmia by their influence on sensory nerves before the true inflammatory dilatation sets

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is seen in cases of embolism of the cerebral arteries (white softening) and of the central artery of the retina.

When an artery becomes blocked in a part (*e.g.* limb), of which the veins are valved, no reflux can occur; but infarction may. It is rare, because such parts have a rich arterial supply, but it may follow blocking of the main artery.

Litten agrees with Cohnheim that the red corpuscles escape by diapedesis, but simply on account of the stretching of the capillaries and small veins by the mechanical congestion. It begins almost at once after the application of the ligature, before anæmia has had time to effect any marked change; and no escape occurs in a kidney shelled from its capsule if a ligature on the renal artery be cut after three or four hours.

Further observations must decide between these two views. With regard to venous reflux, it is hard to believe that Cohnheim was mistaken when he said that he *saw* half of a tongue, of which the artery was tied, fill from the vein. Perhaps the resistance offered by the capillaries of the tongue is less than that of the kidney vessels.

in. This must be included in the next group of cases. But the dilatation characteristic of inflammation is due to direct damage of the vessel-wall, and therefore falls under this heading; and when it is more than sufficient to counterbalance the increased resistance which always accompanies it (see "Inflammation"), the quantity of blood passing through the part will be greater than normal—*i.e.*, the part is hyperæmic. The sudden removal of pressure is another cause of hyperæmia, proved by the congestion of the abdominal vessels which results on the removal of much ascitic fluid, or of a large ovarian tumour; by the bleeding which occurs when a pleura is more or less completely emptied by aspiration or strong syphon-action; and by the hæmorrhage which often follows the complete emptying of a chronically distended bladder. The muscle of the vessels, accustomed to much support, has lost power, so, when the support is suddenly removed, the vessels dilate fully, and small ones perhaps rupture.

2nd. **By the removal of the vaso-tonic action of the sympathetic, either directly or reflexly**—*i.e.*, **by inhibition.** Examples of the direct process are:—the active congestion which follows pressure upon the sympathetic—as in the neck, by an aneurism—or section of vaso-motor nerves in any part of their course, from the centre in the medulla, down the cord, into spinal nerves or sympathetic plexuses. Thus, unilateral congestion results from diseases and experimental sections of half the spinal cord. Certain drugs, taken internally, are believed to temporarily and directly paralyse the vaso-tonic nerves—*e.g.*, nitrite of amyl, alcohol, tobacco.

The reflex process is generally due to stimulation of sensory nerves, the diminution in tonus thus produced being more or less accurately confined to the region supplied by the nerve. Friction and slight irritants in the early stages of their action produce hyperæmia in this way (see above). It seems that vascular dilatation of deep organs may be produced reflexly by the application of stupes to the skin over them.

Anæmia of any large part—as of a limb compressed by Esmarch's bandage, or of the skin from cold—necessarily causes hyperæmia of other parts—**collateral hyperæmia.** But all parts do not suffer equally, as they would were the hyperæmia the result simply of increased arterial pressure; certain vessels, as the great abdominal veins, dilate, showing that the vaso-motor system arranges for the accommodation of the surplus blood by producing local diminutions of vascular resistance. After extirpation of one kidney, its share of blood passes mainly to the other.

3rd. **By excitation of vaso-dilator nerves**, such as the chorda tympani. Nothing is certainly known of this as a cause of hyperæmia; but the hyperæmia associated with facial neuralgia, and that of the thyroid in exophthalmic goître, have been referred to vaso-dilator neuroses, and also to inhibition of vaso-tonic nerves.

RESULTS.—The results of active hyperæmia are principally such as might be expected to follow from an increase in the amount of the arterial blood, and in the rapidity of its flow, in any particular organ or tissue. The symptoms in a superficial part are:—increased redness and pulsation, a sensation of throbbing being often experienced by the patient; some increase in bulk; marked elevation of temperature, sometimes as much as 3° Cent. If the hyperæmia be of long duration, or frequently repeated, the small arteries become permanently enlarged, their walls gradually thicken, and the epithelium and connective tissues of the part increase; as may be seen in the papillary thickening round a callous ulcer of the leg, and the occasional spread of ossification into the granulation-tissue from the tibia. Hypertrophy of other tissues is also a frequent result if they be called upon to functionate. (See "Hypertrophy.") Function is increased, except in organs, as the submaxillary gland, which functionate only in response to nervous stimulation. Thus, in hyperæmia of the nervous centres, we see great excitability, paræsthesiæ of sight and hearing, convulsions, &c. In

In venous hyperæmia, the excess of blood is in the veins and capillaries, and the flow, instead of being accelerated, is retarded. This is so frequently produced by some obvious mechanical obstacle to the return of blood through the veins, that it is often called **mechanical** hyperæmia. The congestion of a finger, produced by a moderately tight band round it, may be taken as the type of such cases.

CAUSES.—Anything which weakens the forces which carry on the venous circulation, or which opposes unusual resistance to this circulation—anything which lowers the blood-pressure and slows the stream—must tend to produce venous hyperæmia. It is evident from the preceding general remarks that such causes may exist in any part of the vascular system—heart, arteries, capillaries, or veins; some having a local, others a general, effect. They may be ranged under two headings—(1) those which **diminish** *vis a tergo*, or force with which the blood should be driven through the veins; and (2) those which **directly impede the return of blood by the veins.**

1. Diminished cardiac power is chief in the first group, and one of the most important causes of mechanical hyperæmia. The motor power of the heart becomes impaired in many of the chronic exhausting diseases, also in the acute febrile diseases, as in typhus and typhoid fever, and in those degenerations of its structure which lead to dilatation of its cavities. In whichever of these ways the *vis a tergo* is diminished, that diminished fulness of the arteries and over-fulness of the veins, which is so familiar clinically as the result of cardiac failure, will be produced. If this condition be of long duration, there is necessarily so much interference with the oxygenation of the blood, with the functions of the

blood-forming organs, and with the processes of digestion and assimilation, that the blood itself becomes deteriorated, and thus by its lagging in every tissue, nutrition in general suffers.

In the arteries the driving force may be weakened by obstruction, total or partial, of an arterial trunk from any cause, or by uncompensated dilatation (p. 211), which is likely to arise from simple atony, or from those fatty, atheromatous, or fibroid changes of the arterial wall, so common in advanced life.

Obstruction to the circulation in capillaries arises mainly from pressure of inflammatory effusions, dropsy, &c., on capillary areas.

With regard to the veins:—absence of muscular contraction, especially in the lower extremity, or such dilatation as produces incompetence of valves, and thus renders muscular action useless as an aid to circulation, is an important auxiliary. So, too, is anything which diminishes the elastic force with which the lung tends to draw away from the pleural-wall, and thus lessens thoracic aspiration. Forcible expiration will replace the normal minus-pressure within the thorax by a plus-pressure, and thus playing wind instruments impedes entry of blood from veins into the heart. Emphysema, effusion of air or fluid into the pleuræ, and large new growths of the lung, act similarly.

When, by the above conditions, variously combined, the circulation is much retarded, **hypostatic congestions** of the posterior edges and bases of the lungs, of the skin over the sacrum, and of other parts kept constantly dependent, occur. Slowing of the circulation causes the veins of distant parts to become especially full. If such a part be also dependent, the pressure (not the driving-force) in its vessels is increased by gravity in proportion to the vertical distance from the highest point of the body, in any given position, to the part in question (p. 210); and if the patient is so weak as to be unable to change his position, this high pressure is constantly maintained—

dilating veins and capillaries more or less fully, and greatly increasing the tendency to leakage through the mal-nourished vessels. Thus the part is redder than normal, and œdematous; also softer. The base of the lung seems but a short way from the heart; it is, however, the point in the pulmonary circulation furthest from the right ventricle, which is weaker than the left in proportion as the resistance which it has to overcome is less. Moreover, in bedridden patients breathing is often very shallow, and the effect of expiration in driving blood on to the left auricle is much diminished (see "Hypostatic Pneumonia.") That dropsy from hydræmia or heart disease begins in the legs of people walking about is also due largely to gravity.

2. Direct impediments to the return of blood by the veins are numerous. The congestion of the chylopoietic viscera which results from the obstruction to the portal circulation in cirrhosis of the liver; that of the lung in mitral constriction and regurgitation; that of the systemic circulation in insufficiency of the tricuspid valve; and that of the lower extremities from the pressure of the gravid uterus on the iliac veins, are a few of the numerous familiar examples of mechanical hyperæmia from this cause.

RESULTS.—Whether there be a direct impediment to the return of blood by the veins or a failure in the forces of circulation, the veins and capillaries dilate, and the blood accumulates in them and moves with diminished velocity. The subsequent changes will depend upon the amount of obstruction to the venous return and the force of the arterial circulation; in other words, upon the injury sustained by the vessel-walls from impaired nutrition, and upon the increase of pressure in the veins and capillaries. The most important of these changes are—the transudation of serum, the diapedesis of the red blood-corpuscles, hæmorrhage, fibroid induration, thrombosis, and necrosis.

1. **Transudation of Serum.**—This is the earliest and

one of the most important results of mechanical hyperæmia. The influence of increased pressure upon the amount of transudation is shown experimentally thus :—Tie the main vein of the ear of a rabbit on each side, and divide the sympathetic in the neck on one side ; the transudation of serum into the ear of that side on which the nerve is divided will be very considerable, whilst on the other it will be slight, or entirely wanting. The serum transudes from the capillaries and small veins, and not from the small arteries, and differs from plasma in being of lower specific gravity, in containing less albumen, and in having very little tendency to coagulate, which is probably due to the small number of white corpuscles present in it. Red corpuscles may be present in small or large numbers—varying directly with the amount of obstruction. The greater the pressure, and the more the nutrition of the wall suffers, the more nearly does the transuded liquid resemble the liquor sanguinis, and the greater is the amount of albumen which it contains. If the pressure be very great it may yield a fibrinous coagulum.

The increased absorption by lymphatics which follows increased transudation from the blood-vessels may be sufficient to prevent any accumulation of serum in the part—as is the case, for example, in the ear of the rabbit, where the main vein is obliterated but the arteries are not dilated (see above). Where the lymphatic absorption, however, is insufficient to remove the transuded liquid, this accumulates and gives rise to **œdema** and dropsical effusion. The amount of transudation will be influenced by the anatomical characters of the tissue, being most in those parts in which the blood-vessels are least supported, as in the subcutaneous tissue, and in tissues which present a free surface, as serous and mucous membranes. A lax and toneless condition of the vessels also will favour transudation.

2. **Diapedesis of Red Blood-corpuscles.**—When the obstruction to the venous return is great, not only does serum transude from the veins and capillaries, but red

blood-corpuscles also escape from the same vessels. This diapedesis of red corpuscles in mechanical hyperæmia was discovered by Cohnheim. It may be observed in the web or tongue of the frog after ligature of the main vein. The red corpuscles accumulate in increasing numbers in the veins and capillaries, the blood-stream in these vessels completely stagnates, the red corpuscles become so closely packed that their individual outlines are scarcely distinguishable, the coherent mass oscillates to and fro with the arterial pulsation, and then suddenly some of the red corpuscles penetrate the walls of the small veins and capillaries and escape into the surrounding tissue. This diapedesis occurs without rupture of the vessel, and if the ligature be removed, the blood again circulates in a perfectly normal manner. The corpuscles appear to be squeezed through the capillary walls as the result of the pressure, and rarely escape in great numbers. Perhaps they pass through the stomata which Recklinghausen has shown to exist between the endothelial elements; but as plasma could easily pass through openings large enough for a red corpuscle, and as the transudation-fluid differs markedly from plasma, Cohnheim considers that the existence of these stomata is not necessary to account for the diapedesis.

3. **Hæmorrhage.**—This is another result of mechanical hyperæmia, which usually occurs only when the obstruction to the venous current is very great. It is probable, too, that the nutrition of vessels and tissues has suffered from long congestion; for very heavy strains may be put upon healthy vessels without their giving way. Those vessels which are the least supported are the first to give way. Hæmorrhage into the stomach in cirrhosis of the liver, and into the lung in mitral disease, are familiar examples of this result.

4. **Fibroid Induration.**—This, which is due to a gradual increase in the connective tissue around the blood-vessels, is one of the most important results of long-continued mechanical hyperæmia. The interstitial

growth leads to atrophy of the higher structures, and thus to impairment of the functions, of the organ. In the stomach, it produces atrophy of the glandular structures; in the kidney, compression of the urine tubes; in the liver, obstruction to the portal circulation; in the heart, diminution in motor power. The alterations which this change produces in the physical characters of the organs—viz., induration associated with abnormal redness, due to the excess of blood or pigmentation from hæmatoidin—are exceedingly characteristic.

5. **Thrombosis,** as a result of mechanical obstruction, will be described in the following chapter.

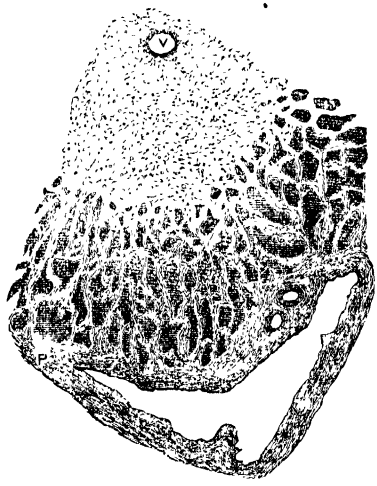
6. **Necrosis** occurs from mechanical hyperæmia only when the obstruction is very general and complete. It has been already described (p. 25).

In addition to the foregoing, long-continued mechanical hyperæmia leads to impairment of vitality and function. The tissues gradually undergo retrogressive changes and atrophy, although from the amount of serosity and blood which they contain, their size and absolute weight may be increased. Their temperature becomes lowered. This form of hyperæmia has no tendency to cause multiplication of tissues other than the connective (fibroid induration), and the epithelial, as seen in catarrhs of mucous membranes.

MECHANICAL HYPERÆMIA OF THE LIVER. —NUTMEG LIVER.—Long-continued mechanical hyperæmia of the liver gives rise to the condition known as **Nutmeg Liver**. This is the condition which so frequently results from disease of the heart. The change is characterised by a large accumulation of blood in the hepatic veins, which dilate and thicken; by atrophy of the hepatic cells in the central portions of the acini; and by increase of the interlobular connective tissue. The impediment to the return of blood by the hepatic vein leads to pressure-atrophy of the cells in the central portions of the acini, and also to the formation of granular pigment, so that when examined microscopically, these

portions of the acini are seen to consist of broken-down cells and granules of pigment. (Fig. 67.) The veins here are found much dilated, and filled with red blood-corpuscles. (Fig. 68.) Their walls are thickened, and there often appears to be also more or less thickening of the intercellular network which immediately surrounds the central vein. Owing to this thickening of the central

FIG. 67.



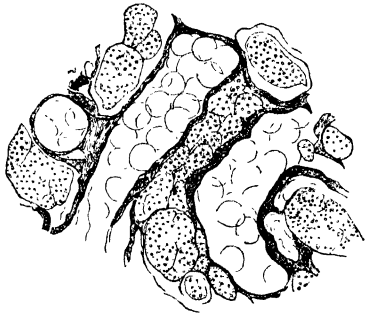
Nutmeg Liver.—Showing the destruction of the liver-cells and the pigmentation of the central portions of the acinus, together with the new growth of connective tissue at the periphery. V. Hepatic vein. P. Portal canal. × 50. (When the specimen is more highly magnified, the peripheral connective-tissue growth is seen to contain numerous nuclei.)

vein and of the adjacent intercellular network, and to the destruction of the liver-cells, the most central portions of the acini, in advanced stages of the disease, may present a fibrous appearance. At the peripheral parts of the acini the new interlobular growth is seen insinuating

itself between the almost unaltered liver-cells. This new interlobular growth is usually distinctly nucleated, but, for the most part, less so than that met with in cirrhosis. Its cellular character has been insisted upon especially by Dr. Wickham Legg.

In the earlier stages of this affection the liver is often considerably increased in size from the large amount of blood which it contains. On section, it presents a peculiar mottled appearance, the centre of the lobules being of a dark-red colour, whilst the peripheral portions are of a

FIG. 68.



Nutmeg Liver.—Portion of Fig. 67, around central hepatic vein (V), more highly magnified. Showing the thickening of the veins, and the accumulation of red blood-corpuscles within them. × 400.

yellowish-white. This latter appearance is often increased by fatty infiltration of the peripheral liver-cells. Ultimately, the organ may undergo a gradual diminution in size. This is due to the atrophy of the cells in the central portions of the lobule, partly from pressure of the dilated central veins and mal-nutrition, and partly from the pressure of the contracting interlobular growth. The interlobular growth tends to cause obstruction to the portal circulation, as in cirrhosis.

MECHANICAL HYPERÆMIA OF THE LUNGS.—In the lungs, long-continued mechanical hyperæmia pro-

duces that peculiar induration and pigmentation which is known as **Brown Induration.** This most frequently results from stenosis and insufficiency of the mitral orifice. The alterations produced in the pulmonary texture consist in the first place of elongation and dilatation of the pulmonary capillaries, so that even in uninjected preparations the alveolar walls appear abnormally tortuous. The epithelial cells lining the alveoli become swollen, probably multiply, and are seen in large numbers, filled with dark

FIG. 69.

Brown Induration of the Lung.—Showing the abnormal number of swollen pigmented epithelial cells covering the alveolar walls, the increase of connective tissue around the blood-vessels, *a*, and the large quantity of pigment. *b*. The alveolar cavity. × 200.

brown pigment, covering the alveolar walls. (Fig. 69.) They frequently accumulate within the alveolar cavities. These changes are followed by an increase in the interlobular connective tissue, by the formation of large quantities of brownish-black pigment, and often by a thickening of the alveolar walls. Sometimes the pulmonary capillaries rupture, and blood is extravasated into the lung-tissue.

Lungs in which these changes are at all advanced present a more or less uniform brownish-red tint, mottled with brown or blackish-coloured specks and streaks. They are heavier and tougher than natural, less crepitant, and upon squeezing them the pulmonary tissue is found to be denser and thicker than that of a healthy lung.

POST-MORTEM APPEARANCES OF HYPERÆMIA.—The post-mortem appearances presented by hyperæmic organs and tissues vary considerably. Very frequently parts which were hyperæmic during life show no signs of it after death. If the blood does not coagulate rapidly, post-mortem contraction of the arteries forces it on into the veins; and thus the recognition of arterial and capillary hyperæmia becomes impossible. The effect of gravitation must also be taken into account in estimating hyperæmia. After death the blood naturally gravitates to the most dependent parts, distending the vessels, now simply elastic:—this is seen in the post-mortem congestion of the posterior portions of the lungs, and of the most dependent portions of the various coils of the intestine The uniform redness of post-mortem staining again, must not be confounded with the redness of hyperæmia. In capillary and arterial hyperæmia, the colour is red, and the injection often presents the appearance of a capilliform network; if very intense it may to the naked eye appear uniform, but a lens will always discover its capillary nature. When the veins are the seat of the hyperæmia the injection is called "ramiform," and the colour is dark blue.

The anatomical peculiarities in the distribution of the blood-vessels will, however, materially affect the appearance of the hyperæmia. In the intestines it is often punctiform, being situated in the vessels of the villi; so also in the kidney, when its seat is the Malpighian corpuscles. A punctiform appearance may be produced also by minute extravasations of blood. If the hyperæmia is of long

standing, the tissue becomes pigmented by the altered hæmoglobin of transuded red corpuscles. This is often well seen in the stomach and intestines ("shorn-beard" appearance); also in the lungs.

CHAPTER XXV.

THROMBOSIS.

THROMBOSIS is a coagulation of the blood within the vessels during life. The coagulum is called a **thrombus**, in opposition to a **clot**—the result of post-mortem coagulation. It may form in the heart, arteries, capillaries, or veins; but is much the most common in the veins.

CAUSES.—The phenomenon of blood-coagulation has been shown by Alex. Schmidt to depend largely upon the white blood-corpuscles. Fibrin is formed by the union of two albuminoid bodies—fibrinogen and fibrinoplastin, and their union is effected by a fibrin-ferment. Fibrinogen exists as such in the liquor sanguinis, but the ferment and the greater part of the fibrinoplastin are contained in the white blood-corpuscles. Destruction of some of these corpuscles, and liberation of the ferment and fibrinoplastin, are therefore necessary for coagulation to take place.

Schmidt has shown also that when blood escapes from the vessels a large number of white blood-corpuscles are at once destroyed. It has further been noticed that clotting during life is associated with abnormality of the wall of the vessel in which it occurs. We suppose, therefore, that fluidity of the blood during life is due to some influence which normal vessel-walls exercise upon white blood-corpuscles, preventing their destruction in any number. Some are constantly being broken up, and a varying—but small—quantity of ferment is always present in the blood; but the vessel-wall has apparently the power of destroying it or inhibiting its action; for coagulation does occur if much ferment is introduced

into, or is formed in, the blood. The nature of this supposed influence of the vessel-wall is quite unknown; but it seems certain that it is exercised by the endothelium —for we know that fatty and calcareous changes of the middle coat do not cause coagulation, whilst atheromatous ulcers, foreign bodies, pieces of new growth, which are all bare of endothelium, do; also that injury to capillaries, which possess only endothelium, causes thrombosis in them.

Prolonged contact with an abnormal vessel-wall will of course favour coagulation, as is well seen in the cure of aneurisms. But **retarded flow** was regarded as an exciting cause of coagulation in apparently normal vessels; and so it is—indirectly. For impaired circulation in a part means damage to its tissues—to its vascular endothelium among others. If the endothelium is kept fairly nourished in spite of stagnation within the vessel, the stagnant blood will not coagulate. Blood within a tied-off turtle's heart does not coagulate till the heart dies. The time before coagulation occurs in the jugular vein of a mammal is longer in proportion to the care with which it is laid bare and the ligatures are applied; and, if this operation be done antiseptically, coagulation does not occur at all. Retardation and even stagnation of flow must therefore be regarded as, at most, but an indirect cause of thrombosis, though it is always a favouring circumstance. **Abnormality or removal of endothelium** is the essential condition. The **causes** producing this are numerous:—

1. **Injuries** — mechanical, chemical, or physical— which destroy or greatly injure the vessel-wall. The most important, because the most frequent of these, are :— section and rupture of vessels, in which thrombosis is the means by which hæmorrhage is temporarily checked; and ligature, torsion, cautery, &c., the means by which surgeons temporarily arrest hæmorrhage which the natural processes are insufficient to stop. All of these, obviously, cause great injury to the vessel-wall. Other examples of such injury are afforded by the action of chemical caustics,

and of the causes of severe inflammations. These latter may be borne to the part by the vessels, and attack them from within; or they may travel along lymphatic spaces, and act on the vessels from without.

2. **The presence in the vascular system of substances not covered by endothelium**:—needles, horse-hair, or wire introduced into the sac of an aneurism, induce clotting upon themselves, as also do already-existing clots (thrombus or embolus), parasites which have penetrated vessels, and new growths which project into the interior of veins.

3. **Such changes in the blood, or in the blood supply of a part, as cause disease of the vessel-walls by imperfect or improper nutrition.** This is a most important group. The simplest of these causes is a tendency to stagnation of blood. This may be due to many causes (p. 218), of which the most important are cardiac weakness, general diminution of vascular tonus, a dilatation (varix) of veins. All these may well be combined in one case to retard the circulation, and thus to produce an abnormal vessel-wall, and prolonged contact of the same blood with it. They are the conditions which give rise to the "marasmic clots" of Virchow. These form in the most dependent veins—*e.g.*, those of the lower limb, pelvis, or back, and in those parts of the heart in which blood tends earliest to remain when the organ does not completely empty itself—viz., the auricular appendices, the apices of the ventricles, and between the trabeculæ. In veins these clots begin just behind the flaps of valves. The force of the venous current being so slight, or the resistance to it being so great, that it no longer completely opens the valves; the blood consequently stagnates, and, after a time, coagulates behind them. Such clots occur in the course of many exhausting diseases—as phthisis, cancer—in which thrombosis is materially facilitated by the quiescent state of the patient. Careful examination of the sites of recent thrombi is said to have demonstrated absence of endo-

thelium; but it might well have disappeared secondarily.

Next come all diseases of heart or vessel-wall which produce loss or impaired vitality of the endothelium. In the heart, inflammation of the endocardium causes destruction of its endothelium, and the growth of granulation-tissue from the opposed surfaces of valves or elsewhere; coagulation is frequent upon these vegetations (see "Endocarditis"). In the vessels, atheromatous ulcers, bare calcareous plates, syphilitic inflammation, and changes due to involvement of veins or arteries in spreading inflammations, may induce thrombosis similarly. Inflammation was formerly regarded as the main, if not the only, cause of thrombosis; hence thrombosis in veins is frequently termed "phlebitis" even at the present day. Inflammation of veins, as already stated, is certainly rare as a *primary* condition, although it not unfrequently results from the formation of a thrombus.

The thrombosis which occurs as an occasional complication of acute specific fevers is explained by the observation of Ponfick that in these diseases desquamation of endothelium may occur over large areas of vessels.

No one who looks at the wall of an aneurism containing clots will doubt that abnormality of wall exists; and the ordinary methods of cure consist in rendering the circulation through it—already slowed by the dilatation—still slower—*i.e.*, in prolonging the contact of the blood with an abnormal surface. In varicose veins, which are frequently the seats of thrombosis, the endothelium can scarcely ever be healthy, though it may not be so defective as to excite coagulation. Here again alteration of vessel-wall is the exciting, slowing of circulation the predisposing, cause of clotting.

4. **Certain conditions of the blood** favour coagulation and promote the occurrence of thrombosis. It is said that the tendency to coagulate is increased in the later months of pregnancy, and after profuse hæmorrhage. To whatever cause it may be due, an increased tendency of

the blood to coagulate is probably never more than a predisposing cause of thrombosis. In septic fevers, thrombosis is not uncommon at points having no direct relation to a wound. Perhaps the blood-state may here assist the other usual causes in the production of a marasmic clot, but it is also possible that organisms may play a part in the process. This seems particularly likely in those frequent cases of venous thrombosis, often going on to puriform softening and secondary phlebitis, which occur side by side with erysipelas, pyæmia, &c., and which have gained for phlebitis a place amongst Hospital diseases.

CHARACTERS OF AND DIFFERENCES BETWEEN CLOTS AND THROMBI.—The ordinary red clot of blood drawn from a vein, the "buffy" clot of inflammation or of delayed coagulation, and the white clot free from red corpuscles obtained by whipping blood with anything having a large rough surface, show the characters and modes of formation of the thrombi with which we have to deal.

Post-mortem coagula in the heart are generally buffy, the thickness of the uppermost pale layer varying directly with the time which elapses before the heart-substance becomes so altered as to allow coagulation to begin. Both in the heart and vessels, coagulation occurs in that part of the blood which is furthest removed from the influence of the wall; hence the smaller the vessel, the later does post-mortem clotting occur. Such clots are soft, watery, never adherent, do not completely fill the vessels, and can be easily drawn out of them as long strings.

Clots formed in the heart just before death connect post-mortem clots and thrombi. These are probably partly due to "whipping" by the chordæ tendineæ, &c., of the blood, which tends to stagnate when the heart is too weak to empty its cavities. As would be expected, they are more or less uniformly decolorised, and, though not adherent, are often so much entangled among the chordæ, &c., that they cannot readily be removed. From their longer dura-

tion and more complete contraction, they are firmer and less watery than post-mortem clots.

Thrombi or ante-mortem clots are of two kinds—**red** and **white**, according as they originate from *quiescent* or *circulating* blood. In the former case, as seen in an artery or vein after ligature, more or less of the stagnant blood on either side of the knot coagulates into an ordinary **red** clot—soft, uniform on section, and adherent to the vessel-wall where this is injured. The thrombus then contracts, still adhering to the wall, becomes drier and less elastic, but is still red. This is the state in which a red thrombus is generally found.

But, when coagulation occurs in blood which is still circulating, as in the sac of an aneurism or on a cardiac vegetation, a **white** or mixed thrombus results. The abnormal surface causes each successive quantity of blood which passes to leave upon it a little fibrin and some of its most sticky elements—leucocytes. If the blood-stream is languid, more or fewer red corpuscles remain in the thrombus, rendering it mixed. These thrombi are **greyish white** or reddish, firmly adherent to the wall, and it is peculiar to them that they are **stratified.** This is probably due to variations in the rate of deposition of the fibrin, in the blood-pressure to which it is subjected, and such like physical conditions.

A thrombus may cause partial or complete obstruction. Once formed, it tends to extend by deposition of more fibrin on its surface. As a rule, this extension is checked by the rapidity of flow at the level of the first large collateral branch in each direction; but sometimes, especially in veins, thrombosis becomes "continued," and one clot may extend from the foot to the cava. Both in arteries and veins, extension is always chiefly toward the heart, though it may occur also in an opposite direction. These thrombi generally adhere to the wall throughout, but sometimes they do so only at their points of origin.

In the capillaries, coagulation occurs only as a result of necrosis or grave injury of the capillary-walls; for they

are so small, that, so long as they are living, their influence in preventing clotting will act upon the whole of the contained blood (Lister); and consequently thrombosis does not extend into them so long as there is sufficient blood-supply to keep them alive.

LATER CHANGES IN THROMBI.—These are:—Decolorisation (when red), resolution, organisation, calcification, softening (simple and infective), and putrefaction.

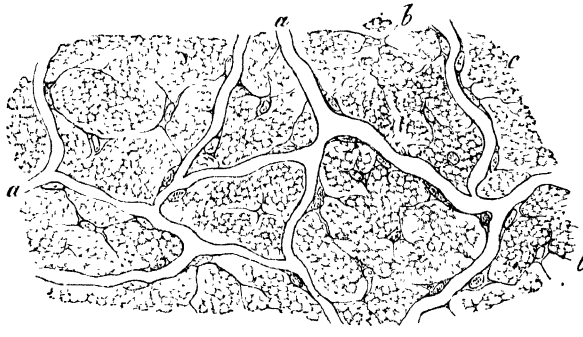
Decolorisation.—The first change in a red thrombus is a breaking-down of the red corpuscles; their stromata become unrecognisable, the hæmoglobin is set free and in great part absorbed, but some may remain as granular hæmatoidin. As a result, the thrombus loses its deep red colour. The process begins in the centre, and takes weeks or months before it is at all complete.

Resolution.—That many thrombi disappear is certain from such facts as repeated bleedings having been effected at long intervals from the same vein, when it was the custom for people to be bled every "spring and fall;" and from the re-establishment of the circulation through superficial veins in the leg or spermatic veins, which are known to have been thrombosed. The steps of the process are not known. In cases of death from septic poisoning, appearances found in vessels which have been tied occasionally indicate that thrombi formed before the onset of the fatal disease have broken down.

Organisation has been studied mainly in thrombi forming as the result of ligature. The effect of the application of a ligature is usually to cut through the middle and internal coats of the vessel; these contract and retract somewhat, turning up and down into the lumen of the vessel; and the constricted external coat is all that is left in the grasp of the noose. In a few hours a red thrombus forms, conical in shape, and adherent by its base to the inverted inner and middle coats. It extends for two or three days, and finally reaches the level of the first collateral branch—often, for some unknown reason, stopping

short of this on the distal side. Meanwhile, it has become firmer, drier, and more widely adherent about its base to the artery. This adhesion progresses as the thrombosed piece of vessel contracts upon the clot, until it becomes universal. By the second day a buffy nodule may be seen in the base of the deep red thrombus, and it rapidly increases, so that in a week or two the colour of the clot has disappeared. After some weeks or months this decolorised plug is found to have been replaced by connective tissue intimately united with the artery, which has the appearance of a firm fibrous cord. The microscope gives the following explanation of the process :—The red thrombus consists of red corpuscles, with a few white, in the

FIG. 70.

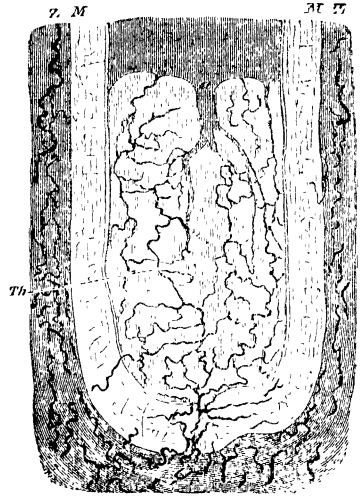


Section of an Arterial Thrombus thirty-seven Days old.—*a.* New blood-vessels. *b.* Leucocytes and anastomosing cells. (Rindfleisch.)

meshes of a fibrin-coagulum. The buffy nodule which grows into the base of the clot is formed of small round cells, which at first are undoubtedly leucocytes migrated from the vasa vasorum injured by the ligature. But there is a difference of opinion as to the origin of those formed after (say) the third day. By this time the cells of the part have recovered from the injury done them by

the wound and ligature; and it is stated by some (Riedel, Cornil and Ranvier) that the endothelial cells multiply and send rod-like processes into the clot, and that these are henceforwards, the source of the invading cells. Others deny this, and maintain that the new cells are all leucocytes. Senftleben secured between double ligatures pieces of vessels, and put them into the abdomens of rabbits. He found that they became filled with connective

FIG. 71.



Longitudinal Section of the Ligatured End of the Crural Artery of a Dog, fifty Days after the Application of the Ligature.—Showing the newly formed vessels in the thrombus and their communication with the vasa vasorum. *Th.* Thrombus. *M.* Muscular coat. *Z.* External coat and vasa vasorum. × 20. (O. Weber.)

tissue containing well-developed spindle-cells, and concluded, therefore, that the development of thrombi during life also depends upon migrated white corpuscles, and not upon the endothelium. Obviously, however, proof

of the ability of white corpuscles to form connective tissue, does not exclude endothelium from doing so likewise as a regenerative process. However formed, the cell-mass is penetrated by blood-vessels, which begin to grow from the capillaries of the vessel-walls on the second day. The cells become spindle-shaped or branched (Fig. 71), fibrillation appears either in them or in the ground substance between them; many cells disappear as the fibres increase, the latter contract, and many vessels are obliterated, the result being—the fibrous cord above mentioned. This is called organisation of a thrombus; but it is evident that the original thrombus disappears entirely, and has nothing to do with the process which goes on in the round-celled mass, of the origin of which we are uncertain. The vessel-wall is converted into fibrous tissue, and blends with that of the clot.

In certain cases, channels are formed in the connective tissue, which communicate both above and below with the lumen of the vessel, and thus the circulation is more or less completely re-established. They are probably due to dilatation of the vessels of the thrombus (though why this should occur in some cases and not in others is unknown), and give rise to the *sinus-like degeneration* of Rokitansky. It is especially common at the junction of the common iliac veins in cases of "white leg," leading to more or less perfect recovery. It is rare in arteries.

Organisation is most frequent in uniform, unstratified thrombi, and especially in those occurring in arteries. But long clots of this kind, such as occur after ligature of the carotid low down, and large laminated thrombi, like those in aneurisms, may long remain as more or less granular masses of non-irritant fibrin, without any sign of organisation.

Calcification.—This occurs in some clots, giving rise to phleboliths. They are especially common in the prostatic plexus.

Softening.—1. **Simple.** A thrombus which undergoes neither of the previously described changes, often softens.

This, in the majority of cases, is due simply to the chemical changes which the constituents of a clot undergo when dead but aseptic, and results in the formation of a more or less fluid, pappy substance, which has a red or white colour according as it originates from a red or white thrombus. To the naked eye in the latter case it looks much like pus, and the change used to be spoken of as suppuration, or **puriform softening**, of a clot. But Virchow pointed out that the fluid consisted of the débris of corpuscles and fibrin—albuminous, fatty, and pigmentary granules. There may be a few recognisable white corpuscles in it, which have probably migrated from without. The outer laminæ generally form a firm case for the softened central part, and if the softening approach the surface, fresh protective clot often forms at the point; but the encasing clot may be perforated and the contents discharged into the circulation. The larger particles will give rise to embolisms, probably too minute to cause symptoms, and circulation is re-established through the thrombus—the process constituting what is known as **canalisation** of a thrombus.

2. **Infective.**—But in certain cases of **puriform** softening, to the naked eye similar to the above, all the symptoms of septic poisoning occur; acute suppurative inflammation of the vein-wall is shown by the microscope; and any portions of the clot which enter the circulation are so intensely irritating as to cause suppuration where they lodge. (See "Pyæmia and Septicæmia.") The difference between the two cases is this:—in the latter form of softening **micrococci** are constantly present, and it is to them that the infective properties of the broken-down clot are due. In the great majority of these cases the veins affected lead directly from a wound, and then the mode of entry of the specific micrococci is evident. In a small number of patients, also with wounds, the thrombosis and softening occur in veins having no kind of direct connection with the wound; here, too, the organisms enter by the wound, and in some cases at least

the thrombosis is secondary to a general septic infection. Finally, there remain a few instances in which no pathological breach of surface could be found for the admission of the germs; it is thought that, in these, they must have passed into the blood through the alimentary or respiratory mucous membranes.

Putrefaction.—This rare change is due to the entry into the clot from some very foul, and often gangrenous, surface of the bacterium termo. The growth of this organism converts the thrombus into a stinking yellow-red fluid, which is highly irritating.

RESULTS.—The results of thrombosis comprise certain changes in the walls of the vessels, more or less obstruction to the circulation, and embolism. These must be considered separately.

1. **Changes in the vessels.**—More or less alteration in the wall of the vessel is an invariable consequence of the formation of a thrombus. When the thrombus undergoes a process of organisation, it becomes, as already described, intimately united with the vascular wall. The latter in the first place becomes infiltrated with cells, and considerably thickened, but ultimately, together with the thrombus, gradually atrophies. It is when the thrombus undergoes a process of infective puriform softening that the most important changes, of an acute inflammatory nature, take place in the vessel. They are due to the irritation of the decomposing thrombus, and are most frequently observed in the veins, where infective thrombi are most liable to occur. The walls of a vein within which a thrombus is undergoing puriform softening are considerably thickened, so that to the naked eye it resembles an artery. The inner surface has lost its translucency, and is of a dead opaque colour. The adventitia and middle coats are injected and present numerous hæmorrhagic points, which are often visible through the intima. The swelling of the wall is due to dense infiltration with leucocytes, which conceals all normal structure; and the innermost cells

die, and are shed into the lumen of the vessel. Small collections of pus may be seen in the external and middle coats. The neighbouring tissue may also become involved. These acute inflammatory changes in veins constitute what is known as **suppurative phlebitis.** Although most frequently due to thrombosis, they may occur also as the result of extension from adjacent suppurating tissues, in which case the thrombus, which also undergoes puriform softening, is *secondary* to the phlebitis. (See "Inflammation of Veins.") Similar changes are observed in the arteries.

2. **Obstruction to the circulation.**—The consequences of the obstruction to the circulation which results from the formation of a thrombus will depend upon the rapidity and cause of its formation, the nature and size of the vessel obstructed, the situation and number of the collateral branches, and the force of the circulating current. The rapidity with which the obstruction is effected is of considerable importance, inasmuch as the more gradual this is the longer is the time allowed for the establishment of a collateral circulation. For this reason the interference with the circulation caused by thrombosis is, for the most part, less marked than that which results from the more sudden obstruction caused by embolism. The cause of the thrombosis is important for the reason already stated—viz., that in that which results from retardation of the circulation the coagulation does not extend into the capillary vessels, unless necrosis occurs.

In the veins when thrombosis occurs in a vessel of small size and when collateral branches are numerous, as in the prostatic or uterine plexuses, the circulation is but little interfered with, and no symptoms of obstruction result. If, however, the main trunk of a large vein, as the ilio-femoral, becomes obliterated, the obstruction is followed by mechanical hyperæmia, the extent and duration of which will depend upon the facility with which the circulation can be restored by the collateral vessels. It must be remembered, however, that the

valves in veins, when they exist, may, by preventing back-flow, offer a great impediment to collateral circulation. Thrombosis in the above-named vein frequently occurs, as already stated, in the latter stages of many chronic debilitating diseases, especially in phthisis; also in the puerperal state, where it gives rise to the condition known as **phlegmasia dolens**. As the femoral is almost the only vein which carries blood back from the lower limb the effect of sudden blocking of it is marked. At first perhaps cyanotic, the limb becomes swollen, pallid white, painful, and too tense to pit; and there is often more or less tenderness along the vein, which feels enlarged, hard and knotty. These symptoms vary greatly in amount; and to them are sometimes added those of lymphangitis and cellulitis. The extent of the thrombus—*i.e.*, the number of collateral branches which it blocks, and the strength of the circulation, will do much to account for the amount of œdema; and it is probable that the more acute inflammatory symptoms are of septic origin. The circulation is usually ultimately restored; but if the impediment has been of long duration, the tissues become thickened, and the limb is left in a hard, indurated, and somewhat enlarged condition.

The results of obstruction in arteries have been already considered in the chapter on Local Anæmia (p. 212). It is in tissues with terminal arteries that the interference is most marked, and here hæmorrhagic infarction, which so often results from embolism, may occur, although owing to the more gradual obstruction of the circulation, it is less likely to do so. (See "Embolism.")

3. **Embolism.**—Portions of the thrombus may be carried away by the circulation, thus constituting embolism. This, which is the most important result of thrombosis, will be considered in the following chapter.

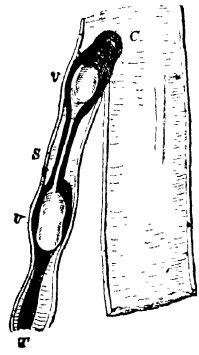
CHAPTER XXVI.

EMBOLISM.

EMBOLISM is the impaction of solid substances circulating in the blood in vessels which are too small to allow to pass. The solid substances are termed **emboli**, and are very various in their nature.

By far the most frequent sources of emboli are thrombi, portions of which are carried from the seat of their formation by the circulation. Emboli may, however, originate independently of thrombi—vegetations and calcareous or atheromatous masses separated from the valves of the heart, or from the inner surface of arteries; portions of new growths, as carcinoma, which, having perforated the vessels, have been carried away by the current; parasites which have made their way into the interior of vessels; fluid fat which has escaped from the fat-cells and entered open lymphatics, as occasionally occurs in fractures of bone, &c.; pigment granules, and other substances, may all constitute emboli.

FIG. 72.



A Thrombus in the Saphenous Vein.—Showing the projection of the conical end of the thrombus into the femoral vessel. *S.* Saphenous vein. *T.* Thrombus. [illegible] *v v*, opposite the valves, the thrombus is softened. (Virchow.)

A thrombus may give rise to emboli in two ways:—A piece may be swept off from a firm, undegenerate clot; or the thrombus may soften, and the results of this process be discharged into the circulation, when any particles too large to pass through the finest capillaries will give rise to embolism. Portions of a parietal thrombus, not filling the vessel, may readily be carried away by the

passing current. Perhaps, however, the most frequent way in which a thrombus gives rise to embolism is by the breaking off of its conical cardiac end which often projects a little way into the cavity, or over the mouth, of a vessel in which the current is too strong to allow of its further progress. (Fig. 72.) Some sudden movement or exertion often determines, in these cases, the separation of the embolus. It is especially venous thrombi which give rise to embolism; the veins of the lower extremity and jugular veins being amongst the most common sources. Emboli from cardiac thrombi are also exceedingly common, whilst those from arterial are the least frequent.

Emboli become arrested in the first vessels they meet with which are too small to allow them to pass. And, naturally, the seat of impaction will usually be at the bifurcation of the vessel, or, where, from the giving off of large branches the calibre diminishes rapidly. (See Fig. 73.) The particles may be so small as to pass through even the finest capillaries, when they give rise to no symptoms; or they may pass through large capillaries, to be arrested in a finer set beyond; but as a rule they become impacted either in the first set of capillaries which they come to, or in some larger vessel between this set and their seat of origin. Thus, emboli originating in the systemic veins or in the right cardiac cavities, will most commonly become arrested in the vessels of the lungs; those originating in the arteries, the left cardiac cavities, or the pulmonary veins—in the systemic arteries and capillaries, especially in those of the spleen, kidneys, and brain; and those originating in the portal venous system—in the hepatic branches of the portal vein. With the exception, therefore, of emboli originating in the portal system, the seat of arrest is the arteries or capillaries.

Emboli are carried usually in the direction of the main current; hence those carried by the aortic stream pass into the thoracic aorta more commonly than into the carotid and subclavian vessels, and into the left carotid and renal

artery than into the corresponding arteries of the opposite side. Gravitation also influences the direction in which they are carried, especially those of large size, which move somewhat more slowly than the blood-stream; hence, they are more common in the lower lobes and posterior parts of the lungs than in the superior and anterior portions of these organs.

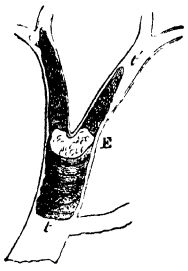
It is not uncommon to find that the finer vessels of an area, of which the supplying artery is plugged, also contain emboli. This may be accounted for in two ways:— If, as is frequently the case, the arrest takes place at a point of bifurcation, the embolus may partially fill both branches, allowing a small stream of blood to pass; this may break off portions of it, and so cause secondary emboli, which become impacted in the smaller divisions of the above main trunks. The second mode is by the detachment of several small emboli from some distant source, which subsequently yields a mass large enough to stick in the main trunk. For it is found experimentally that small bodies injected at intervals into the jugular vein are sometimes swept into the same division of the pulmonary artery.

The amount of obstruction which immediately follows the arrest will depend partly upon the nature of the embolus itself, as well as upon its size and shape. If the embolus be from a soft, recently formed thrombus, it will adapt itself to the cavity of the vessel, and so completely occlude it. If, on the other hand, it is irregular in shape and firm in consistence, as when derived from a calcified cardiac vegetation, it may not fill the vessel, but allow a small current of blood to pass it.

The arrest of the embolus, and the consequent obstruction to the circulation, is followed by the formation of **secondary thrombi** behind and in front of it, which extend as far as the entrance of the first large collateral vessels. (Fig. 73.) If the embolus does not completely fill the vessel, coagulum is deposited in successive layers upon its surface until the occlusion of the vessel is com-

plete, and then the secondary thrombus extends, as in the former case, until it meets with a current of blood strong enough to arrest its progress. If the embolus is a portion of a soft thrombus, it will in most cases be impossible to distinguish it from the secondary thrombus which surrounds it. If, however, it is a calcareous mass, or a portion of an old thrombus, it may usually be distinguished from the more recent secondary coagulum.

FIG. 73.



Embolus impacted at the Bifurcation of a Branch of the Pulmonary Artery. —Showing the formation of thrombi behind and in front of it, and the extension of these as far as the entrance of the next collateral vessels. *E.* Embolus. *tt'.* Thrombi. (Virchow.)

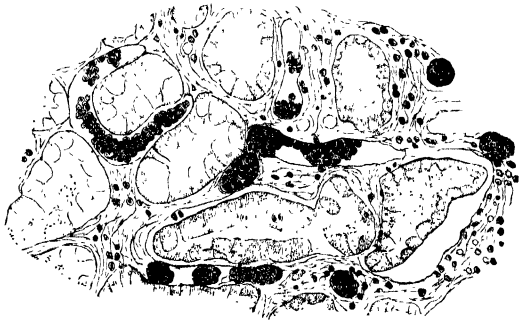
Emboli may, in rare cases, become absorbed. They may also, when derived from thrombi, become organised or soften. The changes in the secondary thrombi are similar to those already described as occurring in the primary (p. 234).

RESULTS.—The results of embolism are of two kinds—those depending upon the simple obstruction to the circulation, and those produced by irritating, or infective properties of the emboli themselves. By "infective" is meant—having the power of setting up in other tissues, changes similar to those going on in the infecting body.

It has already been shown that embolism can occur only in arteries, capillaries, or the portal vein—which differs from an artery chiefly in the lower blood-pressure which exists in it. In the chapter on Anæmia (p. 212), it has been pointed out that simple obstruction of many arteries (as a second or third branch of the mesenteric) or of any capillary is practically without effect upon the circulation, owing to the ease with which collateral circulation is established; that, in other cases, there is more difficulty in effecting this result, and compensation may never be complete; and that, in still other cases, no collateral cir-

culation is established, or can be—from the anatomical and physiological conditions present. Speaking solely of simple, non-infective emboli, their effect when they do not disturb the circulation will be limited to the production of slight irritation of the vessel where they lodge. Such an embolus with its secondary thrombi will usually be absorbed or become organised. That aneurisms, especially of the cerebral arteries in young people, are often due to embolism, is now pretty generally admitted by pathologists. With regard to the mode in which the embolus causes dilatation of the artery, although this may differ

FIG. 74.



Embolic Kidney.—From a case of aneurism of the abdominal aorta. Numerous small yellowish-white patches were seen scattered through the cortices of the organs. × 200.

in different cases, an injurious influence of the embolus upon the walls of the artery, and a consequent inflammatory softening of the vessel, is probably the most common condition.

If an embolus obstructs the supplying artery of a part, and collateral circulation is not speedily established, cessation of function soon follows cessation of nutrition: thus, plugging of one of the larger cerebral arteries is generally followed at once by sudden loss of consciousness and

paralysis (apoplexy); embolism of the pulmonary artery by sudden asphyxia; or of the coronary arteries, by sudden paralysis of the heart.

When emboli block terminal arteries, the result is almost always (Cohnheim) that hæmorrhagic infarction which has been fully described under Local Anæmia (p. 214). The exceptions to this rule are due either to the veins of the part being valved or thrombosed so that regurgitation is prevented, or to the part being so placed that gravity favours strongly the return of blood by the veins; in which cases the area remains pale and bloodless. An apparent exception is owing to the existence of fine arterial anastomoses with certain of a set of arteries, the great majority of which are really terminal; thus anastomoses of the bronchial artery with the pulmonary may sometimes ward off infarction in the lung. One reason why infarcts are so much commoner on the surface than in the substance of an organ is, that in the former situation the whole base is almost absolutely cut off from collateral supply.

The **subsequent changes** which take place in the infarct depend upon its size, upon the extent to which the circulation in it is interfered with, and upon the nature of the embolus which caused the infarction. If the infarct is small and the embolus possesses no infective properties, the coagulated blood gradually loses colour, becoming brown or yellow, the tissue-elements degenerate, and absorption proceeds slowly. When infarction does not occur, and lymph reaches the part in some way from parts around, the cells swell, lose their nuclei, and blend—in fact undergo coagulation-necrosis (see "Diphtheritic Inflammation") and thus form the well-known white wedges. The more external portions of the mass of coagulated blood and necrosed tissue become infiltrated with leucocytes, which develop into fibrous tissue; this contracts, and ultimately a depressed scar may be all that remains to indicate the change. If, however, the infarction is considerable, the central portions may disintegrate and soften. This may subsequently dry up and become encapsuled. For some

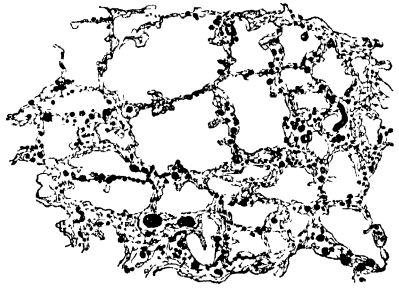
time, whilst these secondary changes are taking place in the infarct, its most external portions are surrounded by a red zone of hyperæmic tissue. This is exceedingly characteristic.

But if an embolus is derived from a part where infective inflammation is going on, it sets up a similar inflammatory process, both in the vessel, within which it becomes impacted, and also in the surrounding tissues. These septic inflammatory changes lead to the formation of abscesses, which are known as **embolic** or **metastatic abscesses**. Microscopic organisms are almost invariably found in these abscesses, and it is to them that the infective properties of the embolus are probably due. No more suitable nidus for their development can well be imagined than a tissue in which infarction and necrosis have occurred, and which is kept moist at the temperature of the body. Infarction, however, is not necessary for the formation of a metastatic abscess. If the metabolism of the tissue in which the embolus lodges does not destroy the organisms, but affords them suitable pabulum, inflammation will ensue. This subject will be considered further in the chapter on "Septicæmia and Pyæmia."

Capillary Emboli.—These generally consist of fat, masses of organisms, clumps of white blood-corpuscles, pigment-granules, or air. In fractures, contusions of subcutaneous tissue, ruptures of fatty liver, acute osteo-myelitis, and other morbid conditions in which fat-cells are broken up and the fat set free, the droplets are absorbed by the lymphatics and veins, especially when pressure in the part is increased by inflammatory effusion or hæmorrhage. Reaching the right heart, they are carried into pulmonary arterioles and capillaries, where their presence may easily be demonstrated by staining with osmic acid. (Fig. 75.) One by one these soft and easily moulded plugs are swept on to the left heart, and distributed by the systemic circulation to other organs, in which also they may be very numerous. For a time, fresh emboli are constantly reaching the lungs; but when this ceases the fat-masses

are passed on to other organs and eliminated, in part at least, through the kidneys. This fat-embolism is believed by some to be the cause of death after simple fractures—a very rare event. But, as large quantities of fat may exist in the lungs and other organs of animals without causing any symptoms whatever, some scepticism is justifiable. If a sufficiently large number of the capillaries of the lung, or any other organ, be blocked by fat, its function cannot be discharged; and in the case of several organs this would mean speedy death. It is probable that the lungs

FIG. 75.



Fat-Embolism of Lung.—From bad compound fracture of leg and severe subcutaneous laceration. The black masses are drops of fat, stained with osmic acid, lying in capillaries and arterioles of alveolar walls. × 40.

always contain, proportionately, many more emboli than any organ supplied by the systemic circulation, and it has been ascertained that half the pulmonary blood-path may be obstructed without disturbing the circulation at large (Cohnheim). We must therefore suppose that, except, perhaps, in very rare cases, the number of plugged capillaries is kept below some point of danger, at present undetermined, by passage of the fat on to the systemic circulation.

Clumps of leucocytes form emboli in septic fevers (Hüter); pigment-granules in ague; and air, in entry of air into veins. Here, as in fat-embolism, the air-plugs

have little effect: death results only from air injected so quickly and in such quantity that the blood in the right heart is churned into foam, upon which the viscus fruitlessly contracts.

THROMBOSIS AND EMBOLISM OF THE BRAIN.

Thrombosis and embolism are the most common causes of **cerebral softenings.**

Softening from Thrombosis.—This is commonly the result of atheromatous, calcareous, or syphilitic changes in the cerebral arteries. Such changes cause a diminution in the lumen, or a roughening of the internal surface of the vessels; impair their elasticity and contractility, and so favour the occurrence of thrombosis. As a result of the interference with the supply of blood, the cerebral substance undergoes a more or less rapid process of necrosis, such as has been already described (p. 70). The softened portions, when recent, and when the obstruction is rapidly induced, are often of a reddish colour, although with age they gradually become decolorised. In the more gradually induced obstructions, the colour of the softened tissue is usually white.

Softening from Embolism.—The softening resulting from embolism is, for the most part, entirely dependent upon the obstruction to the circulation caused by the embolus and by the resulting thrombosis. It is rapidly induced, and is often attended by the extravasation of blood, when it constitutes one form of acute red softening. If the interference with the circulation be slight, there may be no extravasation of blood, and the process of disintegration may be more gradual, so that the softened portions are white in colour, and the condition then more resembles the chronic white softening already described as resulting from degeneration of the cerebral blood-vessels (p. 71). The softened tissue will be white in colour also when one of the large vessels is obstructed, so that a large portion of one hemisphere loses its vitality. The vessel most frequently blocked is the middle cerebral artery, in some part of its course; and in the majority of

cases it is that of the left side. In almost all cases in which softening of the cerebral substance results from embolism, the embolus is arrested in one of the vessels beyond the circle of Willis, because here the circulation cannot be restored by the collateral vessels.

When the interference with the circulation is attended by vascular engorgement and extravasation of blood, the softened portion, in the early stage, is either of a uniform dark-red colour or presents numerous red hæmorrhagic points. The softening is most marked in the centre, whilst the hyperæmia and redness may extend for some distance around it. Under the microscope, the softened portion is seen to consist of broken-down nerve-fibres, altered blood-corpuscles, granules of fat, and the large granular corpuscles already described. (See Fig. 15.) The surrounding capillaries are dilated and filled with coagula, and granular corpuscles envelop their walls. In a more advanced stage all trace of nervous structure is lost, the softened mass becomes decolorised, and passes from a dark-red colour to a chocolate, brown, yellow, or even white. It may liquefy and form a cyst with a fibrous wall; more commonly, however, it is gradually absorbed, being replaced by fibrous tissue, which contracts; and ultimately a cicatrix, with hæmatoidin crystals may be all that remains.

Red softening from embolism is often very difficult to distinguish in the post-mortem room from that which results from thrombosis.

CHAPTER XXVII.

LEUKÆMIA.

LEUKÆMIA, or leucocythæmia, is a disease characterised by a considerable and permanent increase in the number of white corpuscles of the blood, by a diminution in the number of the red corpuscles, and by enlargement

of some of the lymphatic organs. The lymphatic organ most frequently involved is the spleen. This is enlarged in the great majority of cases (Splenic Leukæmia). The enlargement of the spleen is sometimes associated with enlargement of the lymphatic glands, and sometimes, although much less frequently, with an increase in the medulla of bones. In rare cases the lymphatic glands only are involved (Lymphatic Leukæmia), and cases have been described by Neumann and others in which the osseous medulla was principally affected. In most cases of leukæmia an overgrowth of lymphatic tissue in other organs occurs sooner or later in the course of the disease.

Leucocytosis.—Before proceeding with the consideration of leukæmia, it will be well to allude briefly to that slight and temporary increase in the number of white blood-corpuscles which has been termed "leucocytosis." This differs essentially from leukæmia in this respect—that the increase in the number of white corpuscles is only temporary, and is not necessarily associated with any diminution in the number of the red. Further—the increase is never nearly so great as in leukæmia, more than forty or fifty being rarely seen in the quarter-inch field of the microscope. Such slight and temporary increase in the number of white blood-corpuscles occurs in many conditions. Physiologically, it occurs after a meal, and in the latter months of pregnancy. In many of the acute pyrexial diseases, especially in those in which there is acute swelling of lymphatic structures, as in typhoid and scarlet fever, and in septicæmia, there is often a marked excess of white corpuscles. After large losses of blood, also, there is an increase. These conditions are only temporary, and do not appear to interfere either with the circulation or with the general health.

PATHOLOGY.—The pathology of leukæmia is still exceedingly obscure, and will probably remain so until our knowledge of the physiology of the blood and the origin and fate of the blood-corpuscles is more complete. Phy-

siologically, we know that the white corpuscles originate in the lymphatic organs, from which they pass into the blood, either directly or through the lymphatic vessels; and it is now generally believed that the red corpuscles originate from the white, the latter being transformed mainly in the spleen. Owing to the enlargement of one or more of the lymphatic organs which always exists in leukæmia, it has been supposed that the increase in the number of the white corpuscles which characterises the disease, is due to their excessive production by the enlarged organs, such as occurs in some cases of leucocytosis. Inasmuch, however, as there is not only an increase in the number of white, but a diminution in the number of red, this hypothesis is insufficient to account for the blood change. Further—lymphatic organs may become enormously enlarged without the production of any leukæmia. This occurs, for example, notably in the spleen in **Splenic Anæmia,** which disease, with the exception of the increase in white blood-corpuscles, is precisely similar to leukæmia; and also in the lymphatic glands in Hodgkin's disease. Although, as already stated, the subject is still involved in much obscurity, the view promulgated by Virchow more than twenty years ago accounts most satisfactorily for the blood-change:—it is that the normal transformation of white corpuscles into red is imperfectly performed, so that not only is the number of white increased, but that of the red diminished. It is probable that this diminished transformation of the white corpuscles is the most important element in most cases of leukæmia, although it may be associated with an increased production. Both the diminished transformation and the increased production take place in the enlarged lymphatic organs, and all we can say at present in explanation of the process is, that the function of one or

FIG. 76.

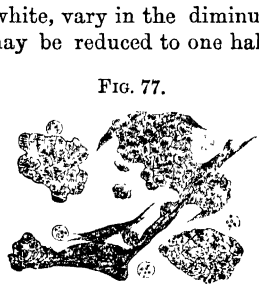
Leukæmic Blood.—From a young man aged twenty-four, with enormous enlargement of the spleen. × 200.

more of these organs is imperfectly performed. The enlargement of the lymphatic organs is, with little doubt, due to new growth, and not, as has been suggested by some, simply to the accumulation within them of the white corpuscles which exist in such large numbers in the blood.

HISTOLOGY.—Blood.—The diminution in the number of white corpuscles varies very considerably in different cases. A proportion of one white to ten red is quite common, and often there are as many as one to three. (Fig. 76.) This increase gives to the blood a paler and more opaque appearance than natural. In the earlier stages of the disease the proportion may not be more than one to twenty or forty. The white corpuscles sometimes resemble the natural ones, but often they are somewhat larger and more granular. This is especially the case in splenic leukæmia, whereas, when the lymphatic glands are principally affected, many of the corpuscles are usually smaller than natural. Some of them are often more or less fattily degenerated.

The red corpuscles, like the white, vary in the diminution of their number. They may be reduced to one half or a quarter the normal. They are usually natural in appearance, but sometimes they are distinctly paler than in health. Occasionally they appear to be unusually soft, and exhibit a tendency to stick together instead of forming the natural rouleaux. In a case of splenic anæmia recently under my care these characters were especially marked. (Fig. 77.) The diminution in the number and the impairment of the quality of the red corpuscles, which exist not only in leukæmia, but in most cases of great splenic enlargement, accounts for the

FIG. 77.



Blood from a case of Splenic Anæmia.—From a middle-aged man with great enlargement of the spleen. × 200.

anæmia which exists in these conditions. In addition to the red and white corpuscles, Klebs and others have found nucleated red corpuscles in leukæmic blood; and minute, colourless, octohedral crystals of an albuminous character have been discovered by Charcot and Zenker in the blood and certain organs. The coagulating power of the blood in leukæmia is much diminished, and when the liquid is allowed to stand the white corpuscles form a creamy layer upon its surface.

Spleen.—In this, which is much the most important organ in the production of leukæmia, the change is characterised mainly by increased growth. The organ becomes enlarged, and usually enormously so. The enlargement is uniform, so that the shape of the organ is but little altered. The capsule is often thickened, and there are usually adhesions with the adjacent viscera. The consistence in the latter stages is commonly distinctly firmer than natural. The cut surface is smooth, of a greyish or brownish-red colour, and thickened trabeculæ can often be seen marking it as whitish lines. The Malpighian corpuscles, although they may be slightly enlarged in the earlier stages of the disease, are seldom prominent, and they are often not visible when the splenic enlargement is advanced. In exceptional cases, however, and especially when the lymphatic glands are involved, they may form prominent growths. Sometimes wedge-shaped masses, of a dark-red or reddish-yellow colour, are seen near the surface of the organ. These are probably infarctions of embolic origin.

When the spleen is examined microscopically, its structure is found to be but little altered, the enlargement being due mainly to an increase of the splenic pulp. The trabecular tissue is also increased and thickened, and becomes increasingly so as the splenic enlargement advances. The Malpighian corpuscles are but little increased in size; sometimes they are atrophied.

Lymphatic Glands.—The enlargement of the lymphatic glands is much less in splenic leukæmia than in those cases

in which the glands are primarily and principally affected. In splenic leukæmia one or more groups of glands are slightly enlarged in about one-third of the cases. The glands are rarely increased in consistence, and are usually freely movable. On section they are of a greyish-red colour, often mottled with hæmorrhages. Microscopically, the enlarged glands present a normal structure.

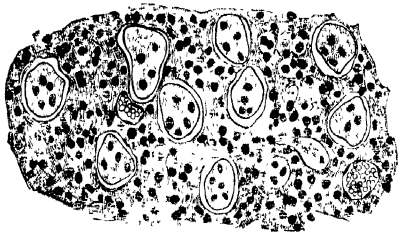
In some cases this excessive development of lymphatic structures takes place in other parts. The **follicles of the intestine** and the **medulla of bone** are those most commonly involved. In the intestines, the follicles may become so much enlarged as to form distinct projections from the mucous membrane, although this is less common than in Hodgkin's disease. The enlarged follicles may also ulcerate. The medulla of bones is occasionally increased, and, as already stated, cases have been described in which this tissue was primarily and principally affected. It is increased in quantity and altered in quality. It is usually softer than natural, and of a greyish or greyish-yellow colour. Microscopically, the fat-cells are seen to be replaced to a great extent by lymphoid elements.

In the course of the disease a new growth of lymphatic tissue or an infiltration with lymphatic elements usually takes place in non-lymphatic structures, principally in the liver and kidneys, less frequently in the lungs and muscle. The new growth in these organs sometimes forms distinct tumours, but much more commonly exists as an infiltration. How far these lymphoid growths are the result of a hyperplasia of the cells in the interstitial tissue of the organ in which they are situated, and how far an emigration of the leucocytes, which exist in such large numbers in the blood, takes part in their formation, is unknown. The former, however, is probably the most important factor in the process.

The organ which is most frequently affected is the **liver.** Here, in leukæmia, the vessels generally are enlarged and distended with white blood-corpuscles. Accumulations of corpuscles and lymphoid tissue are seen between the

acini, and extending along the intercellular network into the acini themselves, so that the lobules are sometimes seen to be clearly mapped out by a greyish-white interlobular infiltration. As this increases, the liver-cells become compressed and atrophy, until ultimately the lobules may be replaced entirely by it. This is well shown in the liver from the case of splenic anæmia, the blood from which is represented in Fig. 77. (See Fig. 78.) Associated with this infiltration there is often a formation of

FIG. 78.



Liver from a case of Splenic Anæmia.—Showing the extensive cellular infiltration involving the intercellular network. The organ was greatly enlarged, and the new tissue was visible to the naked eye between the acini. × 200.

small, round, whitish lymphoid nodules, somewhat resembling grey tubercles. These also are situated in the interlobular tissue. Owing to these changes, the liver becomes very considerably increased in size.

In the **kidneys,** which are also frequently affected, the change is similar to that in the liver. Here also it consists for the most part in an infiltration, with which may be associated the formation of roundish nodules and masses.

CHAPTER XXVIII.

INFLAMMATION.

INFLAMMATION may be defined as "the succession of changes which takes place in a living tissue as the result of some kind of injury, provided that this injury be insufficient immediately to destroy its vitality" (Sanderson).

The exact nature of these changes has been ascertained, for the most part, during the past sixteen years, and chiefly by the experimental researches of Cohnheim, most of which have been repeated and confirmed by Burdon Sanderson. The method of investigation has consisted in the artificial production of inflammation in transparent parts of the lower animals, and observation of the process thus induced. The parts employed have been the foot, tongue, and mesentery of the frog; the tongue of the toad (the best for many purposes), the mesentery of the rabbit, and the wing of the bat. These have shown that the process is essentially the same in warm- and cold-blooded animals; and by microscopic examination of the lip by reflected light, Hueter proved that it is the same in man. The **Process of Inflammation** comprises:—

1st. **Changes in the blood-vessels and circulation.**

2nd. **Exudation of fluid and of blood-corpuscles from the vessels**; and

3rd. **Changes in the inflamed tissues.**

Though thus separated for purposes of description, it must not be supposed that these changes occur in succession in the order in which they are placed; on the contrary, they all go on together.

I. **CHANGES IN THE BLOOD-VESSELS AND CIRCULATION.**—Changes in the blood-vessels and circulation are essential to the existence of inflammation, both in vascular and in non-vascular tissues. In the latter, which comprise the cornea and cartilage, they take place in the adjacent vessels from which these tissues derive

their nutritive supply. Their nature may be studied in the mesentery of a frog which has been curarised; and they may be thus briefly described:—

The first effect of injury of the mesentery—mere exposure to the air being sufficient for the purpose—is to cause **dilatation*** of the arteries, which gradually extends to the veins and capillaries. The dilatation of the arteries commences at once, and is not preceded by any contraction. It steadily and slowly increases for about twelve hours, and is accompanied also by an increase in the length of the vessels, so that they become more or less tortuous. It affects the arteries chiefly, then the veins, and the capillaries but slightly. This enlargement of the blood-vessels is associated at the commencement of the process with an **acceleration** in the flow of blood; this, however, rarely lasts more than an hour, and is followed by a considerable **retardation** in the circulation, the vessels still remaining dilated.

Pulsation is now evident in the smallest arteries; and the stream is slow enough to allow of the distinction of individual corpuscles in the capillaries and smaller veins —perhaps even in the arterioles.

It has, however, long been known that the acceleration of the blood-flow in an injured part—the so-called **determination** of blood, which was so correctly described more than thirty years ago by Dr. C. J. B. Williams—is not constant, and often subsides without the occurrence of any of the characteristic phenomena of inflammation. Cohnheim consequently states that dilatation of vessels with increased velocity of the blood-current ensuing immediately after the infliction of an injury are accidental. In some cases they are followed by contraction, after which dilatation with slowed stream commences. This dilatation with diminished velocity, on the other hand, comes on slowly, is constant, and permanent so long as the cause

* With certain irritants, as ammonia, a short contraction of the arterioles may be the first result.

acts, and must be regarded as the essential vascular change of inflammation.

Returning to the observation of the frog's mesentery—the retardation of the circulation in the dilated vessels is sometimes seen to take place somewhat suddenly, and is usually first observable in the veins. As the stream gets slower, white corpuscles are seen in increasing numbers in the plasmatic layer in the **smaller veins**—rolling slowly along, sticking here and there, and finally coming to a standstill—until these vessels are lined by them as with a spheroidal epithelium (see Fig. 79), often more than one cell in thickness. Some stick also in the capillaries. The time at which this occurs varies greatly; it is the earlier the more severe the injury. This narrowing of the veins by layers of leucocytes, among which there are no red corpuscles, increases the obstruction to the circulation, which becomes slower and slower, both on this account and because the damage is becoming greater; and the red corpuscles, with some white, accumulate in the capillaries, which appear as if distended by a red injection-mass. Actual measurement, however, shows that they are but little larger than natural. After a time, all onward movement ceases in the capillaries, and their contents sway to and fro with the pulse. This is the stage of **oscillation**; and it is succeeded by that of **stasis**, in which no movement of any kind occurs. Finally, **thrombosis** or coagulation may take place, but not until the capillary walls are dead. Thrombosis puts an end to that escape of corpuscles from the vessels which will be treated of in the next paragraph.

II. **ESCAPE OF FLUID AND OF BLOOD-CORPUSCLES FROM THE VESSELS.**—The circulatory and vascular changes have been described from beginning to end, as if they were the only phenomena of inflammation. But this is far from being the case. Soon after the veins become lined by white corpuscles, the field becomes more and more obscured by the presence of small round cells in the substance of the mesentery. At even an earlier period, though the microscope does not show it,

the fluid which naturally escapes from the vessels increases greatly in quantity, and changes in quality. So soon as the lymphatics become unable to carry it off, it accumulates in the connective-tissue spaces, and causes swelling of the mesentery. These finally become insufficient to hold it, and it escapes on the surface together with a number of the small round cells. Here a coagulum forms consisting of fibrin, small round cells, and some red blood-corpuscles. The **false membrane** can be removed, and the field cleared for observation, until another membrane forms.

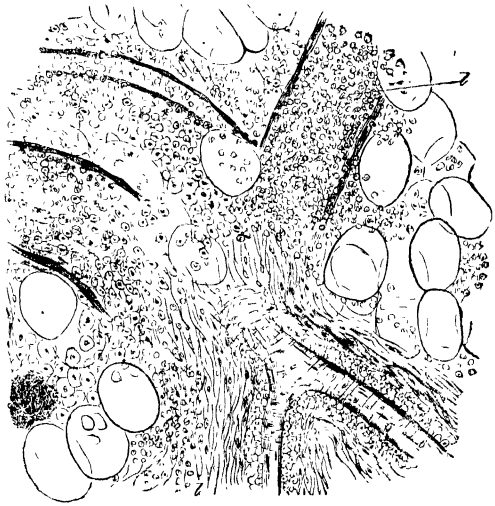
a. **Source of the New Cells.**—If a small vein lined by leucocytes be carefully watched, the following changes will be seen—perhaps at once, perhaps not for some time. Some of the leucocytes immediately adjacent to the wall gradually sink into it, and pass through into the surrounding tissues. Various stages of their passage may be observed. At first, small button-shaped elevations appear on the outer wall of the vessel. These gradually increase until they assume the form of pear-shaped bodies which still adhere by their small ends to the vessel-wall. Ultimately, the small pedicle of protoplasm by which they are attached gives way, and the passage is complete, the corpuscle remaining free outside the vessel. A similar escape takes place, but to a less extent, from the capillaries.

In most inflammations the escape of white corpuscles is far in excess of that of the red; but in the most severe, in which stagnation is induced in a large number of capillaries, the usual state of affairs may be reversed. From such capillaries red corpuscles almost alone pass out, occupy the interstices of the tissues, and give the exudation a hæmorrhagic character; whereas, if the blood is in motion, most red corpuscles pass through the inflamed area whilst the stickier white adhere to the wall. Intensity of injury and vascularity (*i.e.*, number of capillaries) determine the proportion of red corpuscles in the exudation. They pass out chiefly from the capillaries, and several often escape in quick succession from one spot,

giving rise to a red spot, visible to the naked eye as a punctiform hæmorrhage. No rupture of vessel occurs, as may be shown by injection.

Both red and white corpuscles at first remain near the vessels whence they have escaped; but they are pushed away by other corpuscles, washed away by the escaping fluid, and the white corpuscles move away by their peculiar power of locomotion. Thus they may ultimately be found far from their source.

FIG. 79.



Subcutaneous Tissue some distance above dead part in a Case of Spreading Gangrene.—Three veins packed with leucocytes (*l*), which are escaping freely. Round the artery (below) there are none. Many leucocytes outside the vessels have increased in size. × 200.

But are white blood-corpuscles the only source of those numberless cells of embryonic appearance which crowd the tissues in every inflammation other than the most trivial? Virchow advanced the view that they all arose by multi-

plication of connective-tissue corpuscles. Dr. W. Addison, in 1842, inferred from his observations that leucocytes passed through the vessel-walls and became pus-cells; and, in 1846, Dr. Augustus Waller actually saw them escaping, and described and made drawings of the process. Both concluded that the escaped corpuscles became pus-cells; but their observations were unheeded, and it was not until the process was rediscovered by Cohnheim, in 1867, that escape of blood-corpuscles came to occupy an important place in the pathology of inflammation. Cohnheim now asserts that all new cells formed in the tissues as a direct result of injury, are escaped white corpuscles which have migrated to the spot at which they may be found. And, in spite of the opposition of Stricker and his pupils, proof after proof of the correctness of this view has been given. The last stronghold of those who uphold the origin of these cells from multiplying connective-tissue corpuscles was the non-vascular tissues, and especially the cornea. Böttcher showed that after slight central injuries of the cornea, which caused no affection of the surrounding vessels, the sites of the corneal corpuscles in the neighbourhood were occupied by clumps of embryonic cells which he believed could have been formed only by multiplication of the fixed cells. Cohnheim pointed out that the new cells might be leucocytes which had migrated from the conjunctival sac; and Senftleben proved that this was their source. With chloride of zinc solution it is possible to kill the corpuscles in a small central area of the cornea without affecting the marginal vessels, and also without destroying the dense anterior corneal lamina; under these circumstances the spot remains clear, and no clumps of embryonic cells are found. But, if the spot irritated is near the margin of the cornea, the vessels here dilate, and it becomes cloudy from infiltration with leucocytes. And, if to central injury not affecting the vessels a cut or stitch through the anterior lamina is added, opacity results from infiltration of corpuscles from the conjunctival sac.

It will be seen, later on, that all functions of inflamed parts are depressed; it is therefore, *à priori*, unlikely that the cells of an inflamed part would at once begin to multiply. If a cornea, or other piece of tissue, of which the cells are suspected of multiplication, be cut out, kept for days—to ensure its being dead—then rendered aseptic and placed in the peritoneum or subcutaneous tissue of a living animal, all the appearances of multiplication will be found. Lastly, prolonged observation (8 or 9 days) of connective-tissue corpuscles of the toad's tongue (Dowdeswell) has shown the absence of all except degenerative changes. It seems almost certain, therefore, that Cohnheim's view is correct—viz., that all new cells found in inflamed tissues as a direct result of the injury which caused the process are escaped blood-corpuscles. In the less acute forms we find also cells which are formed by regenerative processes going on in the cells of the tissues; but these must be sharply distinguished from those of inflammatory origin (p. 266).

β. **Exudation of Fluid.**—As before stated, one of the earliest effects of the vascular changes in inflammation, is increased exudation of fluid. Something of this was noted in the microscopic examination of the inflamed mesentery, but other experiments show much more. Lassar tied a canula into a large lymphatic of each hind-leg of a dog, stopped the circulation in one leg, and dipped it into water at 54° C., thereby exciting acute inflammation. On removing the fillet the lymph-stream from the canula at once exceeded the normal, and soon reached eight times that on the sound side. At first the fluid was clear; but after a time white corpuscles in increasing numbers made it cloudy, and red corpuscles were found in small numbers. Swelling of the foot began while the flow of lymph was free, evidently because the exudation was too rapid to be conveyed away by the lymph-channels, even when fully dilated. Later in the experiment the flow diminished, partly because exudation diminished as pressure rose, and partly from coagulation

in and blocking of lymphatics. The lymph collected differed from the exudation-fluid in mechanical hyperæmia in containing a much larger proportion of albumen, more phosphates and carbonates, and in having a much greater tendency to coagulation. This latter property is partly due to the greater number of white corpuscles which it contains. The lymph differed from liquor sanguinis in containing distinctly less albuminous material. The composition of inflammatory effusion, however, is not constant. In the most acute inflammations it contains a large number of red corpuscles; in less severe, white corpuscles are in great excess of red. The more severe the process, the more nearly does the fluid approach plasma in its composition and tendencies; whilst in the less severe it becomes very like the fluid in mechanical hyperæmia.

III. **CHANGES IN THE INFLAMED TISSUES.**—It has now been determined that no increased activity, no multiplication of tissue-elements, occurs as a part of the process of inflammation; but that, on the contrary, the process leads everywhere to depression of vitality, degeneration and death. The destructive effect of many inflammations renders this tendency only too obvious. Lister long ago gave the following proofs of depressed vitality in an inflamed part from the earliest stages:—The blood tends to behave as it does in contact with dead tissue; very slight irritation paralyses the pigment-cells of the frog's skin; more severe injury paralyses muscular fibres, for a dilated arteriole in an inflamed area will not contract when a needle is drawn across it; ciliary action becomes excited, and speedily ceases under irritation; the superficial, feebler epidermic cells die and separate after slight injury, which the deeper ones survive. Lister's views as to the nature of inflammation were at the time rejected, because they would not fit in with the cellular theory of Virchow, which required increased activity on the part of the tissues.

The belief that the cells in inflamed tissues originated

by multiplication of the tissue-elements was supported by the fact that clumps of small round cells were always found in the positions normally occupied by the tissue-corpuscles. But these lie in spaces, and migrating leucocytes naturally take the easiest course open to them and invade these spaces. This is proved by the insertion of aseptic pieces of dead tissue into the subcutaneous tissue or peritoneum of a living animal; all the appearances of inflammation will be produced in it, though obviously its own cells cannot have multiplied.

When Senftleben, with chloride of zinc, destroyed all cells in the centre of a cornea without admitting any white corpuscles to the area, the part remained quite clear. On the third day microscopic examination showed that the corneal corpuscles around the damaged area were shooting processes into it; nuclei appeared on the processes, protoplasm collected around them, and branched cells formed, which again threw out regenerative processes; and thus the corneal corpuscles were completely restored. Had leucocytes been admitted to the corneal tissue, controversy would have arisen as to whether they also did not spring from the corneal cells by multiplication; but, inflammatory phenomena being prevented, the regenerative processes could be studied alone. In other tissues also regenerative processes occur—the more resistant elements endeavouring to make good the loss sustained by the tissue; but such attempts are found only in chronic and subsiding inflammations. In these we must be prepared to find evidence of cell-multiplication, but *not* as a part of the process of inflammation. Injury, which causes and fosters the latter, tends to prevent the occurrence of regeneration; the more intense the inflammation, the less likely is evidence of regeneration to be found.

THE ESSENTIAL LESION OF INFLAMMATION.—Having thus briefly described the succession of changes which occur in the process of inflammation, it remains to consider how an injury can produce them. It has been held to cause abnormal conditions of the blood, of the tissues,

of the nerves, and of the blood-vessels. On one, or other, or all of these parts it necessarily must act.

Lister ("On the Early Stages of Inflammation," Phil. Trans., 1858) showed that an irritant did not act through the blood, for momentary approximation of a hot iron could affect but a very small quantity of this fluid. Moreover we can see the circulation going on normally round a microscopic inflammation, whilst corpuscles entering this region tend to stick to each other and to the vessel-walls (p. 261); but, if they get through the part, they go on towards the heart quite normally. Further, blood drawn from an inflamed area behaves exactly like that from other parts.

The tissue-elements are certainly affected in cases due to obvious external injury, but not necessarily, as shown by Cohnheim's experiment of rendering a part anæmic, washing out its vessels with irritating solutions, and then allowing blood again to flow through the part; when all the phenomena of inflammation ensued. It is therefore possible to produce inflammation by injury of the vessels alone; on the other hand, Senftleben's experiments on the cornea (p. 263) show that injury of a non-vascular tissue which does not at the same time affect vessels, is not followed by the phenomena of inflammation.

Sensory and vaso-motor nerves must often be affected by irritants, and no doubt have their share in producing those variations in calibre and flow which often precede the essential phenomena of inflammation. But as all these latter occur with perfect regularity in a part of which everything except the main artery and vein are divided, nerves cannot be regarded as essential to the process.

There remains, then, only the vessel-wall. That this is affected is shown by the facts that all the early phenomena of inflammation are vascular; that injury of vessels alone (Cohnheim) causes these phenomena; that injury of tissues alone (Senftleben) does not cause them. Further, Ryneck has shown that stasis may be produced in the

frog's web in which milk or defibrinated blood is circulating in place of normal blood; and also that in vessels, the vitality of which has been completely destroyed by the injection of metallic poisons, no such stasis can be produced. In all spontaneous inflammations the cause is probably carried to the part by the blood, and acts first upon the vessels, later upon the tissues.

Later investigations have therefore confirmed Lister's conclusion in 1858—viz., that the essential lesion of inflammation was a **change in the vessel-wall** resulting from an injury, which increased the friction naturally offered to the passage of the blood, and was a step towards death. There is no detectable structural alteration of the vessel, however, so Cohnheim speaks of the change as "**molecular,**" and regards it as possibly chemical in nature. To cover all that we now know of the escape of fluid and corpuscles, it is necessary to assume that the molecular change not only increases the friction between the blood and the vessel-wall, but also that it renders the latter more porous.

EXPLANATION OF THE MICROSCOPIC PHENOMENA OF ADVANCING INFLAMMATION.—When **contraction** of arterioles is the first effect of an irritant, it is probably due to its action as a direct stimulant of the vessel-wall.

Dilatation with acceleration of flow may probably occur in two ways. Irritation of a sensory nerve is well known to cause dilatation of the arterioles in its own area of distribution, but heightened arterial tonus elsewhere. The action of an irritant not sufficiently intense at once to directly affect the vessels, will stimulate the sensory nerves and cause this reflex local dilatation. The arterioles dilate and, the blood-pressure being maintained, admit a larger quantity of blood than normal to their capillaries, which cannot dilate proportionally. The blood-pressure in the capillary areas is, *ceteris paribus*, increased as the cross-section of the supplying arterioles increases. Under these circumstances acceleration of

stream will accompany dilatation of vessels. The walls of the latter, being uninjured, may contract after such dilatation. But Cohnheim found that the same phenomena occurred in the frog's tongue, after section of everything except the lingual arteries and veins. They are then due, perhaps, to direct action of the irritant upon the vessel, impairing the contractility of its muscle, but not injuring the endothelium severely. Dilatation of arteries diminishes the resistance, injury of endothelium increases it. If the former is in excess of the latter, the above phenomena will occur. They are not seen in severe injuries, nor from the slow action of croton-oil on a part.

Dilatation with Retardation of Flow.—Retardation soon follows upon acceleration, though the driving force continues unaltered and no contraction of vessels has occurred. Almost the only conceivable cause of slowing is, therefore, increased local resistance, due to alteration in the vessel-wall. It is one of the results of the **molecular change.** Resistance, and therefore retardation, increases with the alteration of vessel-wall until **stasis** and even **thrombosis** are reached.

Escape of Contents of Vessels.—Normally, the vessels permit the escape of the constituents of healthy lymph, cerebro-spinal fluid, the fluid which moistens the pleura, &c. These differ from each other markedly, and we do not know why; but directly an inflammation sets in the normal fluid of the part is changed in proportion to the intensity of the process (p. 265)—the quantity of albumen rises, the tendency to coagulate increases, white corpuscles appear in increasing numbers, red are found in the exudation still later, and are in great excess in the most severe forms of the disease. All this is attributed to the **molecular change,** which renders the passage out of albuminous (colloid) bodies more easy, as has been shown by injecting solutions of such bodies; though the vessels bore the normal blood-pressure without bursting, even after red corpuscles had escaped. The words **migration** and **diapedesis** are unfortunate, insomuch as the blood-

corpuscles seem to take no active part in their escape. Amœboid movements of red corpuscles are unknown, and have never been seen in the white whilst within the vessels. The forms assumed by the latter during their escape suggest that they are forced through by the pressure of a fluid which is also escaping. This is supported by the fact that active migration is at once stopped by compressing the supplying artery. It must not be supposed that they are forced through by *increased* blood-pressure; this is diminished in the capillaries and veins of an inflamed area in proportion as the circulation is slowed by the unusual resistance which it has had to overcome. Cohnheim uses the term "filtration" to describe the process; he says, "Change of filter means change of filtrate." The practical application of the above is either to lessen arterial pressure in inflamed parts, or to counterbalance it by uniform support of the tissues.

Destruction of tissue is due to the damage done to the elements of the part by the injury, to abnormal physical and chemical conditions from exudation, and to imperfect blood-supply in the more advanced stages. It is doubtful whether the leucocytes actually destroy tissue; perhaps their only function is the removal of parts which are dead.

EXPLANATION OF THE CLINICAL SIGNS OF INFLAMMATION.—These are Redness, Heat, Swelling, Pain, and Impaired Function.

Redness and Heat may be taken together, as depending upon the quantity of blood passing through the part in a unit of time. As a rule, this is greater than normal, the excess being most marked in the early stage of the process, when the part is bright-red and hot. Then its vessels are fully dilated, and the resistance but little increased. As the resistance grows, from more marked molecular change and from pressure of increasing exudation, the quantity of blood passing through the part is diminished. Cohnheim measured the blood returning through both femoral veins after inflammation had been

exerted in one foot of a dog. At first the delivery on the injured side was excessive, sometimes more than twice normal; but when diffuse suppuration or sloughing was induced, the delivery became markedly less than normal. Coldness must go with such a state of matters; and the part will be bluish if its vessels are dilated and full, but mottled or pale if they are compressed by exudation. In most inflammations the internal and external resistances to the circulation are not sufficient to counterbalance the dilatation, and the blood-pressure is kept up; consequently, the delivery from the veins remains excessive throughout, and the part is red and hot. Both redness and heat may be concealed by thickness of normal tissues over the inflamed part. An inflamed foot may be several degrees hotter than its fellow, but it is never so hot as the rectum: an inflamed pleura is never hotter than its fellow, but may be colder. The rise of temperature is due merely to more rapid circulation of arterial blood: excess of heat is not produced in the part. Increased nutritive exchange is required to produce heat; depression of function, degeneration, death and absorption, have not this effect.

Swelling, beyond the most trivial, due to dilated vessels, arises from exudation of fluid and corpuscles. It may be entirely owing to fluid, as in hydrocele; or entirely owing to small round cells, the fluid having been absorbed, as in orchitis. It varies in amount with the distensibility of the part, being most marked in such as the scrotum and eyelids, least so in bone. When due to fluid (œdema) the affected part "pits," unless it is very tensely stretched. Swelling from cell-infiltration is firm, does not pit, and is sometimes called "solid œdema." Swelling may be absent in cases of slight inflammation, in which the lymphatics suffice to carry away the increased exudation.

Pain is due to pressure of the effusion on nerve-endings; perhaps also to chemical irritation of them. It is greater the more sensitive and the more rigid the part, and the more rapid the effusion into it, as is seen in

acute suppuration in a digital tendon-sheath. It is often throbbing from the increase of tension with each heart-stroke. The effect of pressure in producing pain is well shown by allowing an inflamed part to hang down.

Impaired function is due to the fact that every tissue is injured by inflammation.

VARIETIES OF INFLAMMATION.—The process of inflammation is always that which has been described on pp. 258–266, no matter what injury may have been its cause; but we find, both experimentally and clinically, that the exudations produced by injuries of different intensity acting for different periods of time, vary sufficiently to allow of a useful classification upon this basis. It will be remembered that the first effect of injury as regards exudation was to increase the quanity of fluid which escaped from the vessels, and to render it more albuminous; then, whilst the rise in quantity of albuminous constituents continued, leucocytes appeared in increasing numbers, and the fluid became more and more coagulable; with the leucocytes came a few red corpuscles, and these in the most intense inflammations, were vastly in excess of the white. These differences in the exudation may be found in passing from the spreading edge towards the centre of an inflammation such as that which constitutes spreading traumatic gangrene. There is no break in the continuity of its production; the passage from serous to hæmorrhagic occurs gradually and *pari passu* with increasing intensity of the injury. Consequently, the following "varieties" are to be regarded simply as steps in the process of inflammation due to variations in (1) the resisting power of the tissues, (2) the intensity of the cause, and (3) the duration of its action.

Serous Inflammations.—As a result of *slight* injury, the normal transudation from the vessels is increased in quantity, and contains excess of albumen, but very few leucocytes. Consequently, it does not coagulate or only a few flakes form. The best examples are chronic

effusions into serous cavities—the pleura, joints, or tunica vaginalis (hydrocele). An effusion of the same kind occurs also in the substance of a part, constituting "inflammatory œdema." Such a part is swollen, "pits" on pressure (unless very tense), and the tissue is found to contain excess of fluid. In impoverished states of the blood, especially when the albumen is diminished, inflammatory exudations, even when the process is of considerable intensity, are liable to be serous. In more intense inflammations also, where the emigration of blood-corpuscles is not fully established, as in the earlier stages of the process, and when the injury to the vessels, although severe, is rapid and transient in its action, as that caused by heat and blistering agents, the effusion is often a clear and only slightly coagulable liquid. With more severe damage the percentages of albumen, fibrinogen and white corpuscles increase, and fibrin forms in increasing quantity. Networks of fibrin are frequent in the meshes of inflamed connective tissue; and large flakes of it may come away in otherwise serous effusions. These inflammations are called **sero-fibrinous** and lead on to the next class.

Fibrinous Inflammations.—In these the exudation is still more richly albuminous and contains more leucocytes; it consequently has a much greater tendency to coagulate, and "lymph" forms on the inflamed surface or in the substance of the inflamed tissue. The proportion of fluid to lymph present in the inflamed part should be small to justify this name. The most typical examples are found on serous membranes. On the surface of the visceral pleura, for example, an irritant produces redness from dilatation of vessels; then follows exudation of fluid and leucocytes, and fibrin forms upon the surface entangling leucocytes in its meshes. Fibrin containing leucocytes constitutes "lymph;" the white corpuscles may be very numerous, or but few may be distinguishable in a granular or obscurely fibrillated matrix. Lymph may now form upon the opposed surface of the parietal pleura,

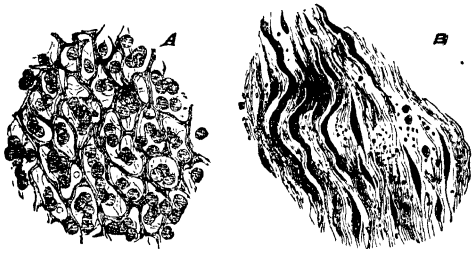
which becomes infected from the original focus, and the two patches blend. This is the first stage in the formation of an "adhesion"—*i.e.*, a band of connective tissue between the two surfaces. Lymph, formed in exactly the same way, is the temporary uniting medium in healing by the first intention; and it is similar lymph which "glazes" the surface of an open wound a few hours after its infliction. In these cases the fluid escapes from the free surface. A similar exudation occurs into connective tissue as a result of chronic slight irritation; the fluid is apparently absorbed as fast as it escapes; fibrin probably forms, but is soon removed by the agency of leucocytes which crowd the tissue and replace those parts of it which have been destroyed by the primary injury and the process excited by it. Such an inflammation may end in absorption—some leucocytes wandering into lymphatics and re-entering the circulation; others, together with the fibrin, undergoing fatty changes and forming an emulsion which is similarly absorbed.

Productive Inflammations.—In many cases the inflammatory process ends in the formation of new tissue—inflammatory connective tissue; and the inflammation is then said to be **productive**. In this case any fibrin present disappears before the leucocytes which crowd into the lymph and convert it into a tissue of closely packed leucocytes in a scanty homogeneous matrix. To supply this with nourishment, vascular loops spring from the capillaries of the inflamed tissue and penetrate into the lymph in all directions; this is **granulation-tissue**—the presence of vessels and of a homogeneous instead of a fibrinous matrix constituting the difference between it and lymph. It derives its name from the fact that on the floor of a healing ulcer, which consists of this tissue, the young cells mass themselves round the apices of capillary loops, all of which project towards the surface; and we thus get the floor made up of rounded projections, about the size of a pin's head, which are called "granulations." (See Fig. 82.) *The plentiful formation*

of vessels is essential to the changes which this tissue undergoes in the production of connective tissue. In healing wounds, new vessels have been found protruding from adjacent capillaries by the end of the second day (Wywodzoff).

The development of granulation tissue into connective tissue has been studied by Ziegler, who placed chambers formed of two slightly separated cover-glasses, in the subcutaneous tissue of dogs, and removed them at varying periods. Up to the fifth day they contained round cells—some with one, others with a bi- or tri-partite nucleus; then there appeared cells twice the size of leucocytes, containing a large vesicular nucleus, slightly contractile, and capable of taking particles into their substance. These are often called epithelioid—a bad name. Ziegler speaks of them as **formative-cells** or **fibroblasts**, because from them all new connective tissue develops.

FIG. 80.



Varieties of new Growth resulting from chronic Inflammation of Connective Tissue. A, an *adenoid*, B, a *fibroid*, structure. × 200.

As they increase in number those with divided nuclei disappear, so it is probable that the fibroblasts feed upon degenerating leucocytes. After the twelfth day giant-cells in increasing numbers were found, formed apparently at the expense of cells in their neighbourhood—either by their coalescence or by their degeneration and absorption

by a single cell. Many giant-cells degenerate, but some may develop into connective tissue. This tissue is thus formed:—the fibroblasts assume very various shapes—pyriform, spindle, and branched—and are closely packed in a homogeneous intercellular substance. The protoplasm of many cells, on the sides of the nucleus and in the processes, fibrillates, and by the union of bundles from different cells and by spread of the process to the intercellular substance, we get wavy, intercrossing fasciculi of fibres, to which adhere some of the nuclei of the original cells with a little protoplasm. (Fig. 80.)

This new connective tissue is called inflammatory or **scar-tissue**. At first it is highly vascular, a recent scar being redder than the surrounding parts; but the tendency to contract is characteristic of this new fibrous tissue, and as this proceeds vessels disappear and the scar, in the course of some weeks or months, becomes white as compared with surrounding parts. This contraction of scar-tissue may produce most serious results, such as the gravest deformities, or atrophy of the essential epithelial elements of glands. (See "Interstitial Nephritis" and "Cirrhosis of Liver.") It is most marked where the tissues are loose, as about the scrotum; and it appears to be essential to the process of healing, which ceases in a callous ulcer of the leg, so soon as infiltration of surrounding tissues and adhesion to deeper parts arrests contraction. A scar is always a weak point in the system, but a tight scar is always irritable and very liable to break down.

But granulation tissue frequently does not develop into scar-tissue. Continuance of excessive irritation, insufficient development of vessels, diminution of their lumina (as occurs in gummata), too dense packing of the cells, and therefore excessive pressure on the vessels, will inevitably lead to degeneration. It has been found that imperfect blood-supply is accompanied by the development of giant-cells; they are found in all truly chronic inflammations. Thus the typical structure of a tubercle

is—a giant-cell in the centre, surrounded by formative (epithelioid) cells, whilst outside these is a ring of ordinary leucocytes. In gummata, lupoid nodules, &c., similar structures are frequent. A section through the thickened synovial membrane in a case of chronic arthritis often shows the following appearances:—Externally, we find ordinary granulation tissue, perhaps developing into scar-tissue; passing towards the joint cavity, we find next a layer of formative cells in which giant-cells become increasingly numerous; yellow spots and patches of fatty degeneration now become frequent, and the surface may be composed of granular débris in which cell-forms are no longer distinguishable. A fluid looking like thinnish pus may occupy the cavity; it contains, however, but few pus-cells, consisting really of fatty granules, formed by degeneration of the superficial cells, suspended in fluid. This is chronic "suppuration" in the knee, and chronic "abscesses" of similar nature may form elsewhere, especially in connection with bone (caries of vertebræ, &c.). On the other hand, excessive irritation or rise in intensity of the original irritation will destroy some of the cells of granulation tissue and will produce inflammation of it with free escape of corpuscles from its vessels—will cause it in fact to "break down into pus." This is best seen when the surface of a healing aseptic ulcer, having a serous discharge only, is acted on for some time by a strong antiseptic; the discharge becomes purulent.

Interstitial is the term applied to inflammations of solid organs of which the manifestations lie chiefly in the connective tissue; they may be acute, running on even to suppuration, but as a rule they are ordinary productive inflammations. In **parenchymatous** inflammations the epithelial elements of the organ show the most marked changes. These are probably of a degenerative and necrotic nature, mixed up with regenerative processes. The essential lesion of the inflammation must, of course, be of the vessels in the connective tissue.

Suppurative Inflammation.—This is a very common

form. In it the exudation contains the same elements as in the fibrinous exudation; the peculiarity of the process is that no coagulation occurs, no lymph forms and vascularises; but any lymph which may have formed at an earlier stage of the inflammation is destroyed when suppuration sets in. The irritant is more intense than that required to produce a fibrinous inflammation, and it is essential that its action be prolonged. Serous and fibrinous stages often precede the suppurative, showing that they are minor grades of the process.

Suppuration may occur in the tissues in either a circumscribed (**abscess**) or a diffuse form, or its seat may be a free surface—mucous membrane or skin. In the latter case, when the epithelium is destroyed with more or less of the subjacent tissues, the process is called **ulceration**, but when the deeper layers of the epithelium remain, it is a **purulent catarrh.**

Formation of an Acute Abscess.—When a suitable irritant acts upon a certain spot of (say) connective tissue, escape of fluid and corpuscles, chiefly white, begins, the corpuscles lying in greatest numbers round the small veins (see Fig. 79) which constitute foci of round-celled infiltration. The infiltration becomes increasingly denser and spreads by migration and transportation of corpuscles until the various foci blend. As a result of the primary injury and of the secondary nutritive disturbance, the tissue-elements die, soften and disappear before the leucocytes. These lie so thickly in the centre of the patch as to seem to be almost in contact, whilst they quickly become few and far between in the surrounding tissues. In the centre no vessels are to be seen, they have first become thrombosed and then have softened and disappeared like the other tissues. No new vessels form. From mutual pressure and from absence of nutrition, the central cells die and degenerate together with the intercellular substance. Thus is formed a cavity, bordered by still living infiltrated tissue, which contains dead leucocytes, fluid intercellular substance and exudation, and a few living cells which have

recently migrated from the living tissues. By thrombosis of vessels and molecular disintegration of the cells they supply, by migration of corpuscles and exudation of fluid into the newly formed space the process spreads, and always in the direction of least resistance—generally towards some free surface, upon which the abscess bursts. We should find on section of the wall of a spreading abscess all the stages of inflammation—a proof of the prolonged action of the cause. In the centre, necrosis; and, in succession as we pass outwards from this, thrombosis, stasis, retardation of flow diminishing, and perhaps giving place to acceleration, before the normal circulation is reached. With retardation begins exudation; much of the fluid is taken off by lymphatics, but the corpuscles accumulate in increasing numbers, and red join the white outside the vessels as the centre is approached. This account explains how it is that we are led to the belief that suppuration has occurred when over a deep-seated swelling we find redness, heat, and œdema—signs of an advancing inflammation—developing.

An acute abscess almost always extends until it bursts or is opened; then tension, a great cause of the continuance of the inflammation is relieved, and the pus formed escapes together with its original cause. If the cavity is completely drained and kept at rest, and the irritation of putrid discharges prevented, the round-celled infiltration of the walls speedily vascularises, and they become lined by granulation tissue. This grows and blends across the cavity, which is perhaps rendered potential by falling together of the walls; and then it develops into scar-tissue, and thus the abscess is healed.

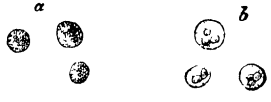
Diffuse suppuration is exactly the same process going on over a wide area. It is often more intense than when circumscribed, and it is by no means uncommon to find shreddy sloughs in the pus—molar death having been the effect of the injury on some portions of tissue.

Pus from a person healthy but for a simple abscess (laudable pus), is a thick, creamy, opaque, yellow-white

fluid, slightly viscid, having a faint odour, alkaline reaction, and specific gravity 1030–1033. It contains 10–15 per cent. of solid matter, of which two-thirds are albumen, and the rest fatty matter and salts, such as are found in blood. On standing it separates into a dense yellow layer —pus-corpuscles, and a clear supernatant fluid—*liquor puris*. The reason why this exudation does not coagulate is unknown.

Pus-corpuscles are spheroidal bodies about $\frac{1}{2500}$th inch in diameter—semi-transparent, more or less granular, motionless, and usually containing a bi- or tri-partite nucleus, the segments of which together are no larger than the original nucleus. Such division is therefore regarded as evidence of degeneration rather than of multiplication and of growth.

FIG. 81.



Pus-corpuscles as seen after death.—*a*. Before, *b*, after, the addition of dilute acetic acid. × 400.

But a small minority of the cells have exactly the appearance of leucocytes, and perform amœboid movements. These are the more recently escaped cells. Acetic acid clears up the cells, and renders obvious the often obscure nucleus (Fig. 81).

It is noteworthy that pus has no power of absorbing sloughs or sequestra; *living* cells are required for this. A bit of bone, even an ivory peg, surrounded by granulation-tissue will be slowly eroded; but it may be in pus for months without losing weight, and suppuration is not likely to cease until it is removed. The prevention of suppuration is therefore to be aimed at in all cases of necrosis and of retention of foreign bodies (especially absorbable ligatures) in wounds.

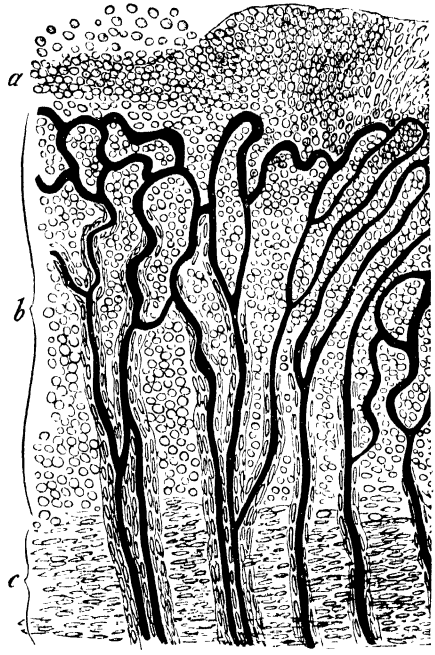
Sometimes, though rarely in the case of an acute abscess, after some pus has formed the irritation becomes so slight that granulation tissue forms round the fluid, and develops into fibrous tissue. The pus may long

remain encapsuled, its corpuscles breaking down into fatty débris; but as a rule the fluid part is absorbed, and a more or less dry, cheesy-looking mass, consisting of cell-débris and cholesterine crystals, is left in the capsule. The mass may calcify. Such collections may lie harmless in the tissues for years, and finally become the centres of fresh suppuration. These changes are much more common in chronic abscesses.

Ulceration.—We have seen that suppuration in the substance of tissues produces molecular disintegration of them; as a rule no distinct slough is found in pus. The same molecular destruction eating away the tissues on a free surface constitutes ulceration. Under the action of an irritant the superficial layer of the skin becomes soaked with fluid, and leucocytes escape in numbers from the vessels and wander even into the epithelial cells, where they seem to have arisen by endogenous multiplication. Under these circumstances the superficial cells do not become horny, and are easily brushed off; or the original irritant may have destroyed their vitality and cohesion, and they are washed away by escaping fluid. The rete is now exposed, and irritation of the deeper tissues more easy by slight friction, contact with chemical irritants, putrid discharges, &c. The inflammatory process becomes more intense, the escape of fluid and leucocytes freer, and stasis and thrombosis occur here and there. Death of portions of the papillary layer and of the covering epithelium follows, they disintegrate rapidly and come away in the discharge. The process spreads by the production of limited stasis and death of tissue; if the stasis is at all widespread, a visible slough will result. It is common, indeed, to see tags of dead tissue adherent to the floor of a spreading ulcer; more intense irritation will at any time render them larger—transform them into "sloughs." Ulceration passes insensibly into gangrene as death becomes too rapid to permit molecular disintegration of the dead parts, as they form, by degeneration

and the action of leucocytes. The discharge in the spreading stage consists of leucocytes and débris of broken-down tissue suspended in fluid. Like the edge of advancing

FIG. 82.



A Granulating Surface.—*a.* Layer of pus. *b.* Granulation-tissue with loops of blood-vessels. *c.* Commencing development of the granulation tissue into a fibrillated structure. × 200. (Rindfleisch.)

suppuration, the margin of a spreading ulcer exhibits all the stages of inflammation, from the mildest to the production of molecular death. An abscess is often described

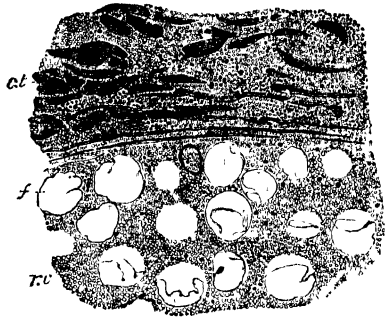
as a closed ulcer. When the causes of the inflammation are removed, the round-celled infiltration of the floor increases and becomes vascularised into granulation tissue (Fig. 82). Sloughs are thrown off by the eating through of their connections with living parts, and soon the base becomes covered with "granulations" (p. 274). These are bright red, slightly raised, rounded elevations, about the size of a small pin's head, and consist of cells grouped round a capillary loop. They contain no lymphatics and no nerves, are not tender, and do not bleed readily. Departure from this type indicates disease of the granulations.

The granulation tissue grows either by multiplication of its cells, or, as some think, by vascularisation of leucocytes, which continue to escape from the newly formed vessels, under the irritation of exposure, dressings, &c.; and it replaces such loss of tissue as has occurred. At the same time all infiltration is removed from the edges, and they sink gradually into the base. Epithelium now shoots in from the epithelial cells at the margin, and three zones can often be distinguished here—an inner, dry, red zone, where the cells are one or two thick; then a wider blue zone where they are thicker, but where no horny cells exist; and lastly, an opaque white ring of sodden horny epithelium. The deeper layers of the granulation tissue are meanwhile becoming scar-tissue, contracting and drawing together the edges of the sore, so the epithelium has less and less to cover; and finally the whole surface is skinned over, and all granulation tissue is converted into fibrous tissue. Contraction goes on even after this, and the resulting scar is very much smaller than the original ulcer.

Hæmorrhagic Inflammation.—This form of inflammaton is characterised by an exudation in which red corpuscles are in great excess. Red corpuscles are the latest to escape of the contents of vessels which we can watch whilst they are subjected to the action of an irritant. In a case of spreading traumatic gangrene, under the

care of Mr. Boyd, the tissues a short distance above the actually gangrenous part were crammed with red corpuscles showing that the vessels could hold none of their contents (Fig. 83); higher up there was a free escape of leucocytes, and of a sero-fibrinous effusion (Fig. 79); and higher still was effusion of simple serous fluid. Of course, the injury may be so intense as to cause free escape of red corpuscles from the capillaries at once. The fluid which soaks the part in these cases is usually thin, and more

FIG. 83.



Deeper layer of Cutis and Subcutaneous Fat a short distance above the dead part in a case of Spreading Gangrene.—The interstices of the tissues are crammed with red corpuscles and a few white. *c.t.* Connective tissue; *f.* fat-cells; *r.c.* red corpuscles. × 200.

or less deeply blood-stained. The greater the number of capillaries present in a tissue, the more likely is an exudation to be hæmorrhagic; severity of injury is the other factor. There are generally many red corpuscles present in the exudation of acute pneumonia. The free escape of red corpuscles shows that the capillary stream in the part is reduced to a minimum, that the injury done to the tissue is a very grave one, and that stasis, death, and thrombosis are impending. Too often obvious gangrene is the termination of such inflammation.

TERMINATIONS OF INFLAMMATION.—1. **Resolution.**—This, the most frequent and most favourable termination of inflammation, consists in the cessation of the process and the restoration of the part to health. For this to occur, it is necessary, first, that the exciting cause be removed; next, that the walls of the blood-vessels be restored to their normal condition, in order that abnormal transudation may be arrested; and, lastly, that all exudation be removed, and killed or damaged tissue-elements regenerated. This restoration will obviously be more easily effected in the earlier than in the more advanced stages of the inflammatory process. But resolution even of stasis sometimes occurs, and may be watched under the microscope. The corpuscles of the stagnant blood move off, one after another, till a slow stream is re-established through the inflamed area; the flow quickens as resistance lessens and as the vessels contract, owing to gradual recovery of their muscular coats; exudation, first of corpuscles, then of fluid, ceases; and the circulation again becomes normal. Serous, sero-fibrinous, and productive inflammations in their early stages are those which end in resolution; once normal tissue has been replaced by granulation tissue or scar-tissue, or has been destroyed by suppuration, ulceration, or gangrene, resolution is impossible. A normal condition of the walls of the blood-vessels is dependent upon the proper circulation of the blood through them and the vasa vasorum. Whatever, therefore, favours the re-establishment of normal circulation in the inflamed area will, as pointed out by Cohnheim, favour resolution.

The last element in resolution is the removal of the inflammatory products—fluid, and corpuscles. These are removed mainly by the lymphatics; but after restoration of the circulation, absorption is carried on to some extent by the veins also. In the later stages of the process any unabsorbed blood-corpuscles or fibrin undergo fatty degeneration, and thus the complete removal of the in-

flammatory products is much facilitated. (See "Grey Hepatisation.") The process of Regeneration will be described later.

All conditions interfering with the lymphatic or vascular circulation, such as the pressure exercised by a large effusion in a serous cavity, or by a richly cellular exudation in a lymphatic gland, must retard resolution. (See "Caseation" and "Scrofulous Inflammation.") Interference with the lymphatic circulation tends especially to prevent absorption, interference with the circulation in the blood-vessels to prevent that restoration of those vessels to a normal condition which is necessary to arrest the continued transudation.

2. **Necrosis.**—Inflammation may terminate in death of the inflamed tissue. Inasmuch as inflammation is always due to injury, the process is probably accompanied, in all but its slightest forms, by death of tissue-elements (Weigert); careful microscopic examination may be necessary to detect this. Clinically, we do not speak of necrosis unless obvious death of tissue has occurred, and generally *en masse* (gangrene), as distinguished from the molecular destruction characteristic of suppuration and ulceration.

The more severe the injury, the longer its period of action, and the feebler the resistance of the tissues, the more likely is necrosis to result. It may be produced in the following ways:—

1. By severe injury acting on a part, not killing it at once, but by continued action producing inflammatory disturbance of the circulation ending in thrombosis. The tissues are affected by the injury equally with the vessels, and suffer also from the circulatory disturbances.

2. By an irritant conveyed to the part by the vessels, affecting them primarily, and inducing the above changes in them. The tissues are affected secondarily, both by the irritant and by the circulatory disturbance.

3. By pressure of inflammatory exudation, fluid or solid, rapidly or slowly strangulating the supplying vessels; as

in sloughing of skin from tense œdema, necrosis of tendons in whitlow, death and degeneration of cells in chronic inflammations. Death is more likely to be produced in this way when the exudation occurs in unyielding parts, especially into bone; here death of the exudation before the bone is completely eroded means death of the bone and formation of a sequestrum.

Some causes of inflammation always lead to gangrene —*e.g.*, those of carbuncle, malignant pustule, hospital gangrene. Such inflammations are sometimes called **gangrenous,** or **necrotic.**

The ulcerative powers by which a slough or sequestrum is detached has already been described (p. 30).

The **Diphtheritic** is a special variety of necrotic inflammation. It affects the surfaces of mucous membranes and wounds. It finds its type in the inflammation of the pharynx and adjacent parts, which characterises the disease "diphtheria." In this the affected mucous membrane is covered by a more or less firmly adherent "false membrane," of grey or yellow colour (sometimes looking like clot from presence of red corpuscles), generally rather tough, but sometimes quite pulpy. Microscopically, it seems to consist of a close network of fibrin, containing here and there leucocytes in the meshes; but the deeper part of the membrane consists of what look like flakes of coagulated albumen. The epithelium is completely destroyed, together with more or less of the sub-epithelial tissue. These false membranes, however, resist much more strongly than fibrin the action of reagents—*e.g.*, acetic acid; and Weigert states that they are formed by "coagulation-necrosis" of the epithelial and connective tissue elements. Certain of these cells are killed by the injury, and Cohnheim supposes that in dying they give origin to a ferment and to a body like paraglobulin, which unites with the fibrinogen of lymph—a hypothesis supported by the fact that the diphtheritic process occurs only in parts freely supplied with lymph, and is arrested

by suppuration, as the formation of fibrin is. When affecting only the epithelial layer of the larynx, the disease is called "croup."

A similar pathological change may occur on any mucous membrane—*e.g.*, conjunctival (diphtheritic conjunctivitis), intestinal (dysentery). These are infective inflammations; but simple injuries, like scalds, will produce the same anatomical change. The existence of a diphtheritic membrane by no means implies the poison of diphtheria as its cause.

Such membranes must be distinguished from those really formed of lymph.

3. **New Growth.**—Inflammations ending in new growth are the so-called "productive" inflammations (p. 274). For this to occur the inflammation must reach the fibrinous stage, it must endure for some time, it must not pass on to suppuration, and the blood-supply must be plentiful.

ETIOLOGY OF INFLAMMATION.—It must always be remembered in considering the mode of production of an inflammation that *there are two factors in the process*—**the cause** and **the tissues** which it acts upon. We have learnt (p. 18) that tissues may either inherit or acquire an impaired power of resisting injury; in this case a proportionally slighter cause will be required to produce the same result.

With regard to the nature of the cause—it is always some mechanical, chemical, or physical agent which injures the vessel-walls, and generally the other tissues also. These agents, if of sufficient strength and continued for a sufficient time, would produce death of the part, and, short of this, they produce changes towards death.

Etiologically, inflammations may be divided into **simple** or **traumatic**, and **cryptogenetic**, including (*α*) **septic**, and (*β*) **infective.**

1. **Simple** or **Traumatic Inflammations.**—These are those due to the action of some obvious, injurious agency, such as mechanical violence, the action of caustic and irritant chemicals, of excessive heat or cold, of electri-

city strong enough to produce electrolysis of the fluids of the part, or of prolonged local anæmia and consequent privation of blood. It is characteristic of inflammation from these causes alone, that it has *no tendency to spread beyond the part originally injured nor to pass on to more advanced stages after the cause has ceased to act.* Every one knows how slight are the inflammatory changes induced by very severe subcutaneous injuries, smashing bones, opening up joints, &c.; but in Man these are almost the only cases in which all other causes are excluded. In animals experiments have furnished us with other proofs.

Hüter injected a five-per-cent. solution of nitrate of silver or of chloride of zinc into muscles and other tissues of animals, quite killing the part acted on. In a large number of the cases no sign of inflammation was found in the surrounding tissues. Other experiments were made by plunging a cautery into a muscle (Hallbauer) and bringing the previously divided skin together over the injury, antiseptics being used. Only such changes occurred round the eschar as take place in the absorption and replacement by fibrous tissue of a simple infarct. Here, then, we have examples of the most severe mechanical, chemical, and physical injuries killing considerable masses of tissue, and yet inflammation does not advance beyond its earliest stages. In each case the irritant, though intense, is fairly localised in its action, which is of short duration. Certain parts are absolutely killed by it, and the area around these, which is damaged, is a very narrow one. So soon as the noxa has ceased acting the tissues tend of themselves to recover; hence inflammation excited by such causes as the above is at its height very soon after the action of the irritant, and tends soon to subside unless some fresh irritant is introduced. A chemical irritant may enter the body at a distance from the part at which its chief action takes place; thus alcohol taken by mouth causes cirrhosis of the liver, and turpentine or cantharides inflammation of the kidneys, by which organs these drugs are eliminated.

Under this heading come inflammations which are referred to cold and wet—"rheumatic" and "reflex" inflammations. When a man gets conjunctivitis from the action of a draught through a keyhole upon his eye, the relation between cause and effect is easily comprehensible; but it is not so easy to understand why a neuritis of the facial should ensue from exposure to cold whilst a great thickness of superficial tissue seems uninjured. But this difficulty becomes much greater when internal organs (lungs, kidneys) become inflamed, apparently in consequence of cold acting upon the surface, of wet feet, &c. Pneumonia, which appeared to be an example of this, seems likely to prove an infective disease. On this view, any effect produced by cold can be regarded only as predisposing. We know that surface-cold drives the blood to internal organs and raises the blood-pressure; can this produce inflammation? Lassar plunged rabbits into iced water and thoroughly chilled them; he found changes in all the organs, especially the lungs and liver, in which the arteries were thrombosed and patches of round cells lay about the veins; the same changes were noted in fœtal organs when the animals were pregnant. He believed the changes to be due to the irritant action of cooled blood upon the vessels of internal parts. Perhaps something of the same kind may occur in man, and a locus minoris resistentiæ must be assumed to explain why the kidney in one case, the lung in another, is affected. Frequent exposure to cold might then well be regarded as a cause of chronic nephritis; for the temporary albuminuria induced in some people by a cold bath shows that the kidneys become much congested.

It is held by some that **excessive functional activity** is a direct cause of inflammation—conjunctivitis from overwork being the usual example.

Nervous Influence, too, called into action by irritative lesions of nerve trunks, is regarded as a direct cause; herpes zoster being the favourite instance. The data are not yet sufficient to decide the question.

Many irritants of the above class act once for all, and, if severe, generally for a short time only; but slighter forms may act constantly or frequently—as a foreign body lodged in the tissues, alcohol, or cold. But, speaking generally, none of the irritants of this class acting under natural conditions produce suppuration. If intense, the animal soon gets away from them; whilst those which do not cause pain are not sufficiently intense to cause suppuration, no matter how they act. Nitrate of silver injected forms an albuminate, and probably soon ceases to irritate; but if glass capsules of croton-oil or turpentine, which are not thus neutralised, are placed aseptically in the subcutaneous tissue and the capsules broken when the wound is healed, suppuration results, and no organisms are found in the pus (Councilman). A condition like this rarely or never arises in man; in him we must look among the next classes for the causes of suppuration.

2. **Cryptogenetic Inflammations.**—In a very large number of the inflammations met with in practice there has been no obvious mechanical, chemical, or physical injury. Until recently the causes of such were obscure, and they have hence been called **cryptogenetic**, a better name than idiopathic. In the chapter on Vegetable Parasites evidence has been given which proves that some, and renders it probable that all, of these inflammations are due to the action of various fungi. These may act either as mechanical or as chemical irritants—essentially, therefore, they produce inflammation in the same way as do the gross lesions which have been mentioned as causes of simple inflammation. But the living and particulate nature of these poisons confers upon the processes to which they give rise so many peculiarities, besides that of obscurity of origin, that they are best treated of separately.

Fungi, by their growth in animal fluids, keep up a continuous supply of the products of their life-action so long as the conditions are suitable for their development.

When the products are irritant, necrosis, or some form of inflammation, will result in the tissues with which they are in contact. The result will vary with the quantity and intensity of the irritant, and the duration of its action. Other features in the morbid process are due to the rate and mode of spread of the organism through the tissues. With regard to the quantity of the poison—the fungus may grow freely or with difficulty, according as the conditions are favourable or unfavourable; in the one case there will be much, in the other little, poison produced. The resistance of the tissues to the same poison varies; hence the variations in intensity of the same disease—*e.g.*, erysipelas. Different fungi give rise to products varying enormously in their power of injuring the tissues—some producing actual gangrene, others the various degrees of inflammation in either an acute or chronic form. It is for the production of those forms of inflammation which require the steady action of an irritant that the fungi are so peculiarly suited; for, so long as they can grow, a continued supply of irritant is kept up. If the irritant is tolerably intense, suppuration is induced, just as it was by croton-oil (p. 292); the strong irritant kills the leucocytes soon after their escape, and in some unknown way prevents the formation of fibrin. If the irritant is less intense, the early stages of productive inflammation (p. 275) results, as in tubercle, leprosy, farcy. The characteristic lesion of these and some other diseases is a tumour-like inflammatory nodule developed round a spot, as there is reason to believe, at which parasites have lodged, and whence they may spread and infect neighbouring and distant parts. These lesions are therefore spoken of collectively as the **Infective Granulomata**, a name signifying infective tumour-like formations of granulation tissue (Ziegler).

With regard to the rate and mode of spread in the tissues—some fungi cannot live in healthy tissues at all (non-pathogenic); of the pathogenic, some spread only by continuity of tissue, others find a suitable nidus in lymph,

and therefore spread by lymphatics (soft chancre poison), whilst others again enter the blood-stream and are carried everywhere by it (Bacillus anthracis). It is in this way that the so-called **metastatic** inflammations are probably to be explained—*e.g.*, the secondary abscesses of pyæmia which constantly contain organisms, the orchitis of mumps, the albuminuria which so often complicates certain specific diseases. Unless organisms *settle* at certain spots they cause no local irritation; but it by no means follows that they can develop and excite irritation wherever they may lodge.

a. **Septic.**—Of **non-pathogenic organisms**, those which cause ordinary putrefaction are of great importance as causes to inflammation. The term **septic** should be limited to inflammations of this kind. When a purely mechanical injury, such as a simple fracture, is complicated with a wound which does not heal by first intention and is not treated antiseptically, more or less profuse suppuration, perhaps spreading widely from the seat of injury and inducing necrosis, results. Often the discharges and sloughs become obviously putrid as the inflammation develops; and the microscope reveals in them Bacterium termo and other organisms, especially micrococci. The chemical products of these fungi are the cause of the inflammation; and, if pent up under any pressure in the wound, they are driven into lymphatics and connective-tissue spaces, exciting inflammation, going on even to sloughing. In tissues thus killed, the non-pathogenic organisms may grow, exciting fresh decomposition in the immediate vicinity of living parts, and thus the process may spread. If all discharge is drained away as fast as it forms, and if there are no sloughs upon the surface of a wound, there will be nothing for a non-pathogenic organism to develop in; for lymph must be regarded as living. Free drainage is not, however, always obtainable, nor can sloughing always be prevented; we must therefore prevent the access of organisms to the dead material by the use of antiseptics about the wound, by filtration

of the air through cotton wool, &c. When this is done the course of an open wound is like that of a subcutaneous injury.

A wound is a spot through which pathogenic organisms frequently enter the body, septic discharges being apparently suitable media for their development. Practically it is found that a wound guarded from putrefaction is protected also from infective organisms.

β. **Infective.—Pathogenic Organisms** cause inflammation by penetrating into **living** tissues, and causing irritant decomposition of their fluids. Their mode of penetration and other facts concerning their life-histories are given in the chapter on Vegetable Parasites; as also are the inflammations of which they are believed to be the cause. They are called **infective** because their poisons multiply in the tissues and spread or are conveyed to neighbouring (locally infective) or distant (generally infective) parts in which they set up similar processes. Simple and septic inflammations are **non-infective**. Peculiarities in the poisons (probably in the life-requirements of the fungi) impart those peculiarities to the inflammations to which they give rise, by which the latter are recognised; and these peculiarities are constant. Such inflammations are called **specific**, because they arise from specific causes.

CHAPTER XXIX.

THE INFECTIVE GRANULOMATA.

The infective granulomata, which include tubercle, lupus, syphilis, glanders and farcy, leprosy and actinomycosis, have many analogies with tumours. They all consist of cells, varying between lymphoid and giant cells in size, lying in a scanty matrix; and the collection of cells presents to the naked eye a more or less defined outline. The lesions therefore resemble sarcomata in

structure. Many of them develop without any obvious cause, and are accompanied by no signs of inflammation; they often persist for long periods, rarely undergoing absorption or development into a permanent tissue, but often degenerating early; and lastly, most lesions of this kind have an **infective** power, disseminating poison by both blood and lymphatic vessels. In all these respects the above-mentioned new formations resemble malignant tumours, but they differ from them etiologically. In the case of some we know, and there is good reason in all for believing, that the tumour-like nodules are products of chronic inflammation, excited by the growth of organisms at certain points in the tissues. Irritation is maintained so long as the fungi grow, and therefore the processes are often chronic. Vascularisation is imperfect or absent, so degeneration is the rule. Infection of other parts is due to spread of the organism, not of the new cells, from the primary focus.

The above diseases are as specific as the "acute specifics." Their essential lesions necessarily have a decided resemblance; but the primary seats, modes of generalisation, modes and times of degeneration, and the clinical symptoms, establish the most distinct diseases. The transmissibility from person to person of syphilis and glanders is well known; experimentally tubercle can be transmitted, and the clinical evidence in favour of the communicability of this disease and of leprosy is getting stronger. Actino-mycosis has been transmitted from man to animals. The name adopted for the group originated with Virchow, and is used by Ziegler. It seems better than any other to express the nature of the lesions—tumour-like bodies, consisting of granulation tissue, and locally or generally infective.

TUBERCLE AND TUBERCULOSIS.

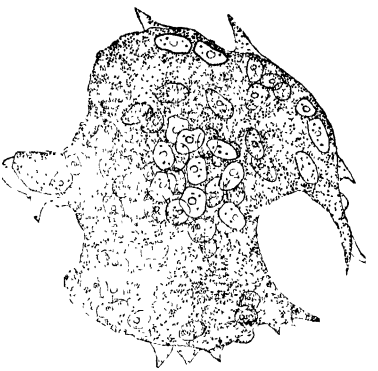
By "tuberculosis" is understood an infective disease, which is characterised anatomically by the formation of those small nodular lesions known as **tubercles.** The

distribution of these lesions may be more or less general—**acute general tuberculosis**; or they may be limited to small areas—*e.g.*, synovial membrane of a joint or a pleura—**local tuberculosis**. The latter, as a rule, runs a much more chronic course than the former, and perhaps its chief danger is, that it may serve as a focus for general infection.

Naked Eye Appearances.—Tubercles are divided into **grey** and **yellow**, the latter being later stages of the former. **Grey,** or miliary tubercles (grey granulations), are greyish, semi-translucent, rounded bodies, varying from just-visible points to nodules the size of a pin's head, or sometimes larger. **Yellow** tubercles are generally larger—sometimes forming masses the size of a cherry or small walnut, and softer than the grey. In some cases most of the tubercles present are grey, whilst in others all are yellow; but it is frequently possible to trace every stage in the formation of a yellow from a grey nodule. Fatty degeneration commencing centrally is the main cause of the difference between them. The larger masses of yellow tubercle are formed, not by growth of individual tubercles, but by the origin close together of several tubercles which blend. It is often possible to recognise a narrow gelatinous zone, which consists of undegenerate tubercles round the cheesy mass, and tubercles may be seen radiating from the cheesy focus into the surrounding tissues.

Seats.—The mucous membranes—respiratory, alimentary, and genito-urinary—and the serous membranes are very commonly affected; so also is the pia mater. The dura mater, the ependyma, and the endocardium rarely suffer. Of the organs—tubercles are frequent in the lymphatic glands, lungs, liver, spleen, kidneys, and testes; less common in the brain and spinal cord, adrenals and prostate; rare in the heart, salivary glands, and pancreas; very rare in the mamma, ovaries, thyroid, and voluntary muscles. They have often been found in skin and bone. They occur especially in childhood and early adult life, but no age is exempt.

FIG. 84.



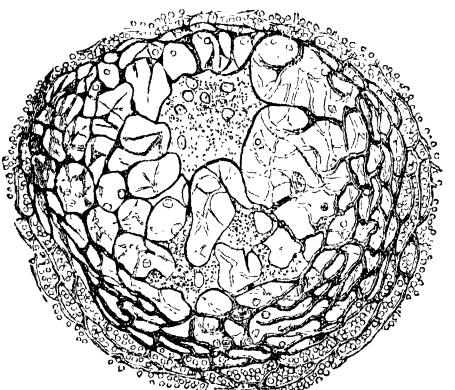
A Multinucleated Cell from the Lung in a Case of Chronic Phthisis.—Showing the large number of nuclei with bright nucleoli. × 400.

FIG. 85.

A Multinucleated Cell from the Lung in a Case of Chronic Phthisis.—Showing the long branched processes, which are continuous with the reticulum of the surrounding indurated growth. Some of the processes are in connexion with smaller nucleated elements. × 200.

Histology.—On examining microscopically even the smallest visible tubercle, it is found to be formed by the aggregation of more minute bodies, each of which as a rule contains the following elements:—Centrally, either one or more multinucleated **giant-cells** (Figs. 84 & 85), or some granular débris surrounded by giant-cells; outside the giant-cells are usually, but by no means invariably, seen large cells with big nuclei and granular protoplasm, often called **epithelioid cells**; and outside these again there is a zone of **lymphoid** elements, which has no definite external or internal limit. The giant-

FIG. 86.



Multinucleated and Branched Cells from a firm Grey Miliary Tubercle of the Lung in a Case of Acute Tuberculosis.—Wide meshes are seen in the immediate vicinity of the cells enclosing a few lymphoid elements. The branched processes are directly continuous with the reticulum of the tubercle. × 200.

cell or cells in many cases send off processes which anastomose and form an open network (Fig. 86), in which the other cells, especially the epithelioid, lie. The lymphoid cells are commonly contained in the

meshes of a homogeneous or more or less fibrillated reticulum, which, in some cases, especially in slowly developed lesions, is well marked (Fig. 87), in others is less prominent, whilst in others again is entirely wanting.

FIG. 87.

A portion of a Grey Miliary Tubercle of the Lung.—Showing the reticulated structure often met with in these nodules. × 200.

The above elements are just those which Ziegler found between his glass plates in chronic inflammations (p. 276). There is nothing specific in any one of them—*i.e.*, no tubercle cell, as was formerly supposed; but the larger forms are commoner in tubercle than in other chronic inflammations—perhaps because tubercles are **non-vascular.** In the pia mater, it is true, tubercles are generally found upon one side of or surrounding a small vessel, lying within its sheath, and often occluding its lumen; and sometimes compressed vessels can be seen lying between the outermost cells. But no new vessels are formed, and those natural to the part, unless they are of some size, are soon occluded by pressure. It will be remembered that the development of giant-cells in inflammatory exudations occurred inversely as the development of vessels; and that imperfect vascularisation led to those degenerative processes which are so characteristic of tubercle. Miliary tubercles are so small that they may well be nourished for a time by surrounding vessels.

A non-vascular nodule of the above structure is the anatomical characteristic of tubercle, and it is not microscopically distinguishable from the products of other very local chronic inflammations. Nor can it be said to be even constant. For, especially in acute cases, soon ending fatally,

some of the tubercles may consist of small round cells—no epithelioid or giant-cells having developed; and in the lung the alveolar epithelium often enters largely into the constitution of the lesions. Tubercles visible to the naked eye will, however, generally consist of aggregations of nodules of the above structure. (See Fig. 97.)

The virus of tubercle does not always produce nodules. Laennec divided tubercular lesions into the **nodular** and the **infiltrating.** In the latter case a diffuse inflammation is found, and microscopic examination shows the presence of numerous non-vascular collections of cells, not aggregated into visible nodules, but separated by an ordinary round-celled infiltration. The presence of the ordinary tubercles in a tissue always excites more or less inflammation, as is best seen in serous membranes.

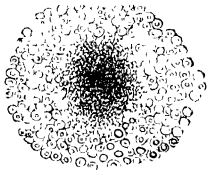
The **sources of the cells** in tubercle have been the subject of much controversy, some maintaining that they are the results of hyperplastic processes among connective tissues (endothelium of lymphatics and serous membranes, adventitia of vessels, ordinary connective tissue), others that they are, or develop from, white corpuscles. Ziegler's experiments incline us to the belief that the latter are the true sources. But the irritation is so slight that regenerative processes may go on in the more resistant cells of the part, and in the ungs multiplication of epithelium takes place freely. Giant-cells are stated by Klein to originate in the lung from the alveolar epithelium. Cheyne also asserts that in the lungs and liver both epithelioid and giant-cells are formed from epithelium as a rule; but the endothelium of the lymphatics may also give rise to them.*

Not long ago tubercle was supposed to arise in lymphoid tissue, but the above statements show that many doubt its origin even in connective tissue.

* *Practitioner*, April, 1883, p. 310.

SECONDARY CHANGES.—Tubercle invariably undergoes more or less retrograde metamorphosis, although the extent of this varies considerably, and in some cases the nodules may become developed into an imperfect fibroid structure. The occurrence of retrograde metamorphosis is mainly owing to the obliteration of the blood-vessels which accompanies the growth of the lesions. The change commences in the centre of the nodule, this being the part first developed, and consequently that which is the furthest removed from vascular supply. The nodule breaks down into a granular fatty débris, so that its central portions soon become opaque and yellowish. (Fig. 88.) In some cases the process of disintegration is rapid, whilst in others it is more gradual. It is usually most marked in the larger and more diffused lesions, and hence it is these lesions which are most commonly of a yellow colour and soft consistence ("yellow tubercle"). In other cases the retrograde change is less marked, the reticulum of the nodule becomes denser and more fibroid, and although the imperfect fibroid tissue usually ultimately undergoes, in its central parts, more or less fatty metamorphosis, the nodule may remain as a firm fibroid mass. This occurs more especially in the smaller lesions. The extent and rapidity of the retrograde change depends, I believe, partly upon the intensity of the infective process, and partly upon constitutional conditions. The existence of scrofula favours retrograde changes in tuberculous lesions, as it does in all inflammatory products, and it is in those who are markedly scrofulous that tubercle undergoes the most rapid degeneration. (See "Scrofulous Inflammation.") These changes will also be

FIG. 88.



One of the Grey Nodules from the Lung in a Case of Acute Tuberculosis, which is becoming opaque and soft in the centre. (Diagrammatic.)

influenced by the intensity of the infective process. The more intense the process the greater is the tendency to the degeneration and softening of the nodules, the less intense and more chronic, the more liable are the miliary lesions to become fibroid.

The retrograde changes of the tubercle may lead to **caseation, calcification,** or **softening**. The occurrence of softening in superficial lesions, as of the skin or mucous membrane, causes the destruction of the covering tissue and the formation of an ulcer. The products of the tubercular process escape and the ulcer may heal; but very frequently the destruction of tissue is kept up by the formation and softening of new tubercles in the base and round the margins of the ulcer. When this process of softening takes place in the substance of an organ, a tubercular abscess results, as is often seen in lymphatic glands, spinal caries, &c. Softening of tubercular masses in the lung gives rise to cavities.

Recovery of a part may therefore occur, with loss of substance, by means of the fibroid change or by the healing of a tubercular ulcer. On the other hand, tubercular processes may directly lead to death by generalising, or by exhaustion from profuse and prolonged discharge, coupled with lardaceous degeneration, or indirectly by opening the way for the infective diseases of wounds—pyæmia, erysipelas, &c.

ETIOLOGY AND GENERAL PATHOLOGY.—Some twenty-five years ago, Buhl, who had noticed the very frequent presence of one or more caseous foci in cases of general tuberculosis and who had described also the local infection which often occurs round such foci, promulgated the view that a poison capable of giving rise to tuberculosis was generated in the process of caseation of the products of some simple inflammation. Caseation was essential to, and was the cause of, the development of the virus. From the centre of its development, the infective material might spread to the neighbouring parts or to parts at a distance.

In 1865 Villemin placed tubercular material beneath the skin of rodents, and general tubercle developed; he believed, therefore, that tuberculosis was a disease due to a specific poison contained in the foci of the disease. His experiments were repeated by Cohnheim and Fränkel, Wilson Fox, Sanderson and others, who found that tuberculosis could be induced, not only by the inoculation of cheesy material which was not tubercular, but also by inducing simple inflammation by the insertion of setons, of vaccine virus, bits of cork, paper, &c. Sanderson, however, concluded that nothing induced tuberculosis with such certainty as material taken from an undoubtedly tubercular source.

Klebs pointed out the possibility of the contamination of the supposed simple material by tubercular, for at that early date precautions were not very stringent. It is probable, too, that in many cases where septic materials were used that the process induced was pyæmic.

In proof of the truth of Klebs' objection, Cohnheim failed to obtain positive results in Kiel and Breslau, his previous experiments having been made in the pathological institute at Berlin; and Fränkel also failed in a private house in the same city. Whilst inoculation of non-tubercular material into the anterior chamber of the eye failed invariably to induce tuberculosis, the inoculation of tubercular material produced tubercles in the iris and in the body at large a little later.* Tappeiner and others caused animals to inhale tubercular material and they became tuberculous. These and other facts caused many to regard tubercle as a specific infectious disease; Cohnheim adopted the view warmly.†

Many of those who held this belief suspected that the virus was a vegetable parasite and searched for it. Klebs,‡

* Cohnheim and Salomonsen: *Virchow's Archiv*, lxxxii. p. 355.
† "D. Tuberkulose v. Standkunkt d. Infectionslehre," 1879.
‡ *Prag. Med. Wochschr.*, 1877.

Schüller,* and Toussaint† cultivated a coccus form from human tubercle and produced tuberculosis by inoculation of animals with it. Schüller found these cocci in chronically inflamed synovial membranes and lupus-tubercles.

Aufrecht‡ stated that the centres of tubercles consist, not of caseous material, but of cocci singly and in chains and of narrow rods, half as long again as broad, stained by fuchsine (in too weak a solution to stain Koch's bacillus).

The next publication was Koch's paper.§ By a special process of staining he first demonstrated the constant presence of peculiar bacilli in eleven cases of acute tuberculosis, twelve of cheesy broncho-pneumonia, one of tubercular nodule in the brain, and two of intestinal tuberculosis in man. Ten cases of perlsucht, and cases of spontaneous tubercle in monkeys and other animals were investigated with a like result; and finally the bacilli were found in a large number of rodents and five cats artificially infected. As proving that the tuberculosis resulted from the inoculation and was not accidental, we have the invariable coincidence; the more rapid development of the artificial than of the spontaneous tuberculosis; the early infection of the glands nearest the seat of inoculation, whereas the bronchial glands usually enlarge first in spontaneous disease; and, lastly, control-experiments in which animals were treated exactly as inoculated animals were, but no **living** bacilli were introduced—no tuberculosis occurred.

Finally, the bacilli were cultivated at 37°–38° C. in blood serum sterilised and rendered solid by a special process; after passing through many flasks, these bacilli suspended in distilled water and injected, produced tuberculosis as surely as the original material.

* "D. Skroph. u. tuberk. Gelenkleiden," 1880.
† "Comptes Rendus," 1881.
‡ "Path. Mittheil," 1881.
§ "D. Ätiologie d. Tuberkulose:" *Berl. Klin. Wochschr.*, No. 15, 1882.

These results have been fully confirmed, especially by Cheyne,* so the proof appears to be complete.

With regard to the cocci found by previous observers—they have not been found by the most eminent workers in the field of micro-organisms; and Cheyne, who obtained material from Toussaint for a full investigation of his results, was unable to confirm them in the slightest degree. On the contrary Koch's B. tuberculosis was the only organism he could demonstrate in tubercles artificially induced by Toussaint.

We are therefore justified in believing that B. tuberculosis is the cause of all tubercular processes. Its presence, at least in the early stages, rather than any anatomical structure, must be the essential characteristic of tubercle.

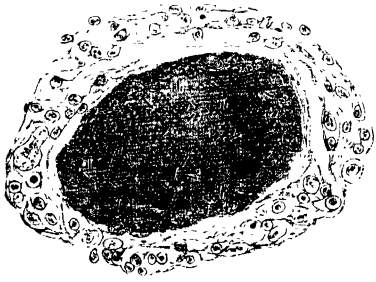
Characteristics of Bacillus.—The bacillus is 2–6 μ long, very thin ($\frac{1}{5}$th–$\frac{1}{6}$th length), motionless, rounded at the ends, and generally appears beaded—clear spots (4–8) alternating with stained parts. They are usually straight, but may be curved; they occur singly, but sometimes in pairs. They probably multiply from spores only within the body. As a rule, they are found in the cells of the tubercle, especially giant-cells. They are well shown here in the accompanying drawing, made from a specimen kindly lent me by Mr. Watson Cheyne. (Fig. 89).

Growing only at high temperatures (30°–41° C.), they probably do not multiply outside the body, but live a wholly parasitic life. They are destroyed by boiling, by perchloride of mercury solution, and carbolic acid; but they resist the action of a 1 per 1,000 solution of the perchloride and a 5 per cent. solution of carbolic acid for some minutes. Drying does not kill the organisms. They may be found in air expired by phthisical patients. Nothing is known of their origin or habitat external to the body. They probably are carried directly from patient to patient.

Mode of Entry into Body.—Nothing is known of their

entry by wounds, though it has been said that tuberculosis has been conveyed by vaccination. The evidence is of the usual *post hoc* kind, and the statement has probability against it; for the blood of tubercular animals is infective only in the most acute cases of general tuberculosis. Post-mortem wounds have never been suspected as a source. The mucous membranes must therefore be the ordinary seats of entry of the bacilli. The success of inhalation experiments with tubercular sputa, and of feeding experiments with tubercular material, demonstrates the entry of bacilli into the respiratory and intestinal mucous membranes, and the possibility of general infection by these channels. The relative frequency of

FIG. 89.



Tubercle Bacilli in Giant Cell.—From Tuberculosis of Horse. × 600.

pulmonary tuberculosis as a primary lesion would go to show that the bacilli enter the system through the pulmonary more often than through the intestinal mucous membrane. But this evidence is not altogether sound; for the primary lesion may occur in a bone, joint, or testicle, not having been preceded by any marked disease of lung or alimentary track. Here it is impossible to say where the bacillus entered; but it must have done so without causing any, or only the most trivial, disturbance. Lymphatic glands are among the commonest primary seats of tubercular disease (*see* "Scrofula"), and as a rule

some irritation in the area whence they derive their supply is discoverable. This may have been actually excited by the entry of the organism, but there is as yet no proof of this; if due to other causes, the damaged tissues would surely admit the bacillus more easily than healthy ones.

Infection through the alimentary canal is believed by some to be brought about by the use of meat and milk of tubercular animals. Perlsucht is very common among cattle, and would be a frequent cause of tuberculosis were infection by this channel easy. Animals fed on the pearl nodules become tubercular; but animals fed on the flesh and milk of tubercular oxen sometimes become tubercular, sometimes they do not. Probably, the bacilli are inconstantly present. The evidence is sufficient to render care obligatory, especially in the selection of milk for children.

Having entered the tissues, the bacillus, either at the spot of entry or at some other spot to which it has been carried by the lymph- or blood-stream, may develop and excite inflammation; or, perhaps, it may find no place in which it can live, and soon perish. Many people are almost constantly exposed to infection through the lungs, and yet do not acquire the disease; and we do not know whether in these cases the organism cannot enter, or enters but cannot live; although the latter is much the more probable. Nothing, however, is more certain than that a certain **predisposition** is almost as necessary for the production of a tubercular process as is the cause. We have no knowledge of what constitutes this predisposition. It may be either acquired or inherited; and affects certain tissues and organs much more commonly than others (p. 297).

Supposing the bacillus to enter and to find a suitable nidus in the lungs, intestine, some lymphatic gland, bone, or joint, it develops and excites a local tuberculosis, the products of which generally caseate more or less completely. Such disease may long remain limited to the

parts first affected, caseating, calcifying, and softening; or recovery may occur. On the other hand, the virus may spread to surrounding parts by means of the lymphatics, or may become generalised by the blood stream, then exciting general acute tuberculosis in suitable subjects.

Modes of Spread. By Lymphatics.—Round a cheesy patch in the lung or brain, grey granulations are often seen extending radially into the healthy tissues; they are most numerous in the immediate neighbourhood of the caseous nodule, and by degenerating and blending with the cheesy focus they cause it to "grow." The situation being a favourable one for observation, the process of infection of mesenteric glands from an intestinal ulcer may sometimes be traced by tubercles along the track. Ponfick has described as not very uncommon in cases of acute tuberculosis, tubercles in the thoracic duct; these he regards as evidence that the virus had passed by this channel to the blood.

By Veins.—Müigge* described tubercular infiltration of the walls of pulmonary vessels, especially veins, in pulmonary tuberculosis; and Weigert† believes that this actual growth of the bacillus into the circulation is frequently the source of general infection.

By Arteries.—In a cheesy bronchial gland from a case of acute tuberculosis Koch found the wall of an artery, which was still pervious, similarly infiltrated; and he believed this to be the source of general infection.‡

In one or other of these ways, or perhaps in all of them, the virus reaches the blood and is carried all over the body, developing when and where the conditions are suitable—in the lungs, meninges, &c. If the supply of virus is plentiful, the case is likely to be most acute. Laennec used to teach that the tubercles appeared in crops, distinguished by the amount of degeneration they had undergone. This would indicate an intermittent supply.

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* *Virchow's Archiv*, vol. lxviii. p. 242.
† *Ibid.*, vol. lxxvii. p. 269. ‡ Cheyne, p. 292.

It is impossible to explain why some tubercular processes remain local, whilst others generalise. Blocking of lymphatics, non-invasion of the walls of blood-vessels, feeble local growth of the bacillus, healthy resistance on the part of the tissues in general, may afford hypothetical explanations.

Although in the great majority of cases of acute tuberculosis a primary cheesy focus is found, it will have been gleaned, especially from Koch's experiments with pure cultivations, that caseation has nothing whatever to do with the production of the tubercular virus.

TUBERCULOSIS OF THE PIA MATER.

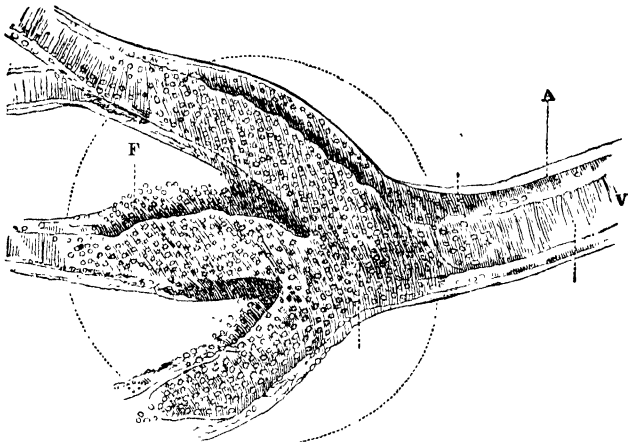
In the pia mater the tuberculous process is associated with inflammation of the meninges, constituting the condition known as **tubercular meningitis**. This is almost invariably a part of a general tuberculosis.

The process is almost exclusively confined to the pia mater at the base of the brain, and the tuberculous nodules—which may easily escape observation—are seen in connection with the small arteries in the Sylvian fissures, and deeply seated between the convolutions. A few scattered granulations are, however, frequently visible on the upper surface of the hemispheres. The inflammatory growth originates in the perivascular lymphatic sheaths which enclose the small arteries of the pia mater (Fig. 90); and the cellular infiltration commencing at separate centres, numerous small grey nodules are produced around the vessel. These, which are distinctly visible to the naked eye, cause an external bulging of the sheath, and a diminution in the calibre, or even complete obliteration, of the enclosed vessel.

The localised obstructions to the circulation which result from the pressure of the perivascular nodules increase

the hyperæmia at the base of the brain, which thus becomes exceedingly vascular, there being in some cases rupture of the vessels and extravasation. A transudation of the liquor sanguinis takes place from the hyperæmic and injured vessels, blood-corpuscles escape, and thus the meshes of the pia mater become infiltrated with a serofibrinous, and often purulent liquid.

FIG. 90.



Miliary Tubercle in the Pia Mater.—The dotted line indicates the original size of the tubercular nodule. A. The lymphatic sheath. V. The blood-vessel. F. Elements within the sheath. × 100. (Cornil and Ranvier.)

These changes in the pia mater at the base of the brain are attended by softening of the immediately subjacent cerebral substance, which becomes infiltrated with young cells. The lateral ventricles at the same time become distended with serum (acute hydrocephalus), so that the convolutions on the surface of the hemispheres are seen to be much flattened. The ependyma and choroid plexus also become exceedingly vascular, and the walls of the

ventricles, together with the fornix and soft commissure, become much softened. All of these changes are owing, partly to an inflammatory process, and partly to the mechanical obstruction to the circulation caused by the tuberculous growth. In addition, the arachnoid membrane is dry and sticky.

TUBERCULOUS MASSES IN THE BRAIN.—In addition to the miliary lesions occurring in the pia mater in tubercular meningitis, large tuberculous masses are occasionally met with in the brain unassociated with a general tuberculous process. These masses, which vary in size from a hazel-nut to a hen's egg, commonly occur in the cerebral substance, especially at the base of the brain. They are of a pale yellow colour and firm consistence, and usually form quite round globular tumours. Their surface is often seen to be covered with minute grey nodules, which extend into the surrounding tissue; and on section, similar nodules are sometimes visible, scattered through the substance of the tumour. In most cases only one or two such masses are found, but occasionally they are more numerous. They occur especially in childhood, and usually in "scrofulous" children. When examined microscopically they are found to be made up of small-celled structure and giant cells, such as has been already described as so characteristic of tuberculous lesions. This structure—which is best seen in the peripheral portions of the tumour—is often concentrically arranged around blood-vessels, and is found undergoing in different parts fibrous and caseous metamorphosis.

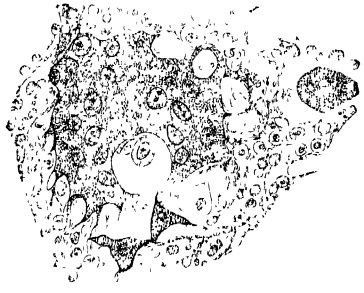
From the fact that miliary nodules are so often to be seen on their surface and extending into the surrounding tissue, it is supposed that these masses originate by the aggregation of such nodules—that the primary nodule constitutes a locally infective focus, and so causes a succession of growths in its immediate vicinity. Occasionally the tuberculous mass causes a more general in-

fection, and so gives rise to tubercular meningitis or to a general tuberculosis (p. 309).

TUBERCULOSIS OF LYMPHATIC GLANDS.

In the lymphatic glands, tuberculous processes give rise, in the first place, to changes in the central portions of the gland (Treves), inasmuch as it is with these that the infective material which is conveyed by the lym-

FIG. 91.



Tuberculosis of a Lymphatic Gland.—The earliest stage of the process, showing the giant cell. × 200.

phatic vessels first come into contact. (Fig. 91.) In the earlier stage of the process small grey nodules are visible, scattered through the cortex. These gradually increase in size and become caseous. The gland then becomes enlarged, the distinction between its medullary and cortical portions becomes lost, and it becomes changed to a greyish homogeneous mass, in which are varying sized tracts of caseous material. The new growth very frequently undergoes a marked fibroid development, so that the caseous masses are surrounded by a dense fibroid structure. The caseous portions of the gland may subsequently soften, dry up, or calcify.

TUBERCULOSIS OF MUCOUS MEMBRANES.

Tuberculous processes in mucous membranes appear often to be secondary to some simple inflammation of the membrane. The intestinal, the urino-genital, and the respiratory mucous membranes may all be the seats of tuberculosis.

THE INTESTINE.—In the intestine the changes have their seat in the solitary and Peyer's glands, and, as in typhoid fever, it is especially these structures in the lower part of the small intestine and in the cæcum which are affected.

The first stage of the process consists in a cellular infiltration of the structure. In Peyer's patches this usually affects isolated follicles in the patch. The solitary glands and certain follicles in the patches thus become swollen, and project with undue prominence above the surface of the membrane. The new elements then undergo retrogressive changes—they soften, the dege-

FIG. 92.

A Tubercular Ulcer of the Intestine. (Diagrammatic.)
a. Epithelial lining. *b.* Submucous tissue.
c. Muscular coat. *d.* Peritoneum.

neration in the patches commencing at several separate centres, and often extending until the whole patch becomes destroyed. As the result of these changes an ulcerated surface is produced, the floor and edges of which are more or less thickened, owing to the extension of the infiltration into the submucous connective tissue. In the floor of this ulcer small nodules of new growth are developed, principally around the blood-vessels, and as these are arranged transversely around the intestine, the new growth proceeds in the same direction. These nodules also soften and become caseous, and thus the process of ulceration gradually extends transversely until the whole circum-

ference of the gut may be destroyed. The ulcer thus produced presents a strong contrast to that of typhoid. Its edges and base are thickened and indurated, and the tuberculous nodules, tending to become caseous, are seen scattered in its floor. (Fig. 92.)

The tubercular ulcer rarely, if ever, heals. Owing to the thickening of the tissues at its base, perforation is quite an exceptional occurrence. In the process of its extension the ulceration is attended by some contraction and narrowing of the gut.

TUBERCULOSIS OF THE LUNGS.

Tuberculous processes occur in the lungs as a part of a general tuberculosis, and also in pulmonary phthisis. The nature of the resulting inflammatory lesions is similar in both. It will be well, however, in the present place, more particularly to describe these lesions as they occur in the general infective disease. The more limited processes which take place in phthisis will be again referred to in a subsequent chapter devoted to the consideration of this affection. (See "Pulmonary Phthisis.")

The pulmonary lesions met with in general tuberculosis consist, for the most part, of disseminated nodular growths, which are universally known as miliary tubercles. These growths are of two kinds—the **grey** and the **yellow**. The **grey** are semi-transparent nodules of a greyish-white colour, varying in size from a small pin's head to a hemp-seed. They are somewhat spherical in shape, and usually possess a well-defined outline. Sometimes they are firm, and almost cartilaginous in consistence; whilst in other cases they are much softer and almost gelatinous. These softer forms, instead of being semi-transparent, are more opaque and white. The **yellow** are, for the most part, larger than the preceding, many of them much so, some being as large as a pea. They are also softer in consistence, less defined and regular in outline, and they pass more insensibly into the surrounding

tissue. Many of them possess a greyish-white translucent margin, which may be pretty firm in consistence, but never so hard as are many of the grey nodules, whilst their central portions are opaque, yellowish, or caseous.

Both the grey and the yellow nodules are often found associated in the same lung; in other cases the grey nodules only are met with; whilst, less frequently, nearly all the growths are of the yellow variety. The condition of the pulmonary tissue which is situated between the nodules varies considerably. It may be perfectly normal, more or less congested and œdematous, or it may present varying sized tracts of greyish, granular, friable consolidation. A perfectly normal condition of the intervening pulmonary tissue is found in many of those cases in which all the growths are of the firm, grey variety; but when there are numerous yellow or soft grey nodules the lungs are nearly always more or less congested or consolidated.

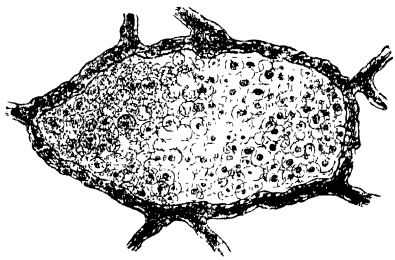
When these nodules are examined microscopically they are seen to exhibit two different kinds of structure—viz., the lymphoid structure with giant cells, which has been already described as that which is the most characteristic of tuberculous lesions, and accumulations of epithelial cells within the pulmonary alveoli (catarrhal pneumonia). There is, however, this marked difference between the various kinds of nodules—that whereas the smaller firm grey ones are constituted almost entirely of the first-named structure, the larger soft grey, and most of the yellow ones, consist largely of the intra-alveolar accumulations.

Firstly, with regard to the soft grey and yellow nodules:—Most of these when examined with a low magnifying power present the appearance represented in Fig. 93, the nodules evidently consisting largely of accumulations within the alveolar cavities. When more highly magnified their constitution becomes more apparent. It is then seen that the alveolar cavities are filled with epithe-

FIG. 93.

ft Grey Tubercle from the Lung in a Case of Acute Tuberculosis.—The whole of the tubercle is shown in the drawing, and it is obviously constituted largely of *intra-alveolar* products. × 100, reduced to ½.

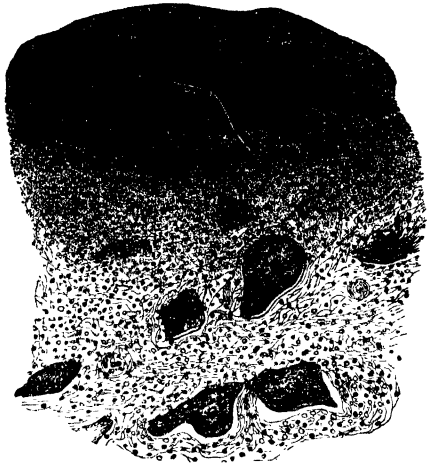
FIG. 94.



A portion of a small soft Grey Tubercle from the Lung.—This is from a case of acute tuberculosis, probably in an earlier stage than that from which Fig. 93 was drawn. The figure shows one of the alveoli filled with epithelial elements and a few small cells, with some cellular infiltration of the alveolar wall. × 200.

lial elements and small cells resembling leucocytes, whilst the alveolar walls are more or less extensively infiltrated and thickened with lymphoid cells. (Fig. 94.) In many cases the central portions of the nodules will be seen to have undergone extensive degenerative changes, and to consist merely of a structureless granular débris, so that

FIG. 95.



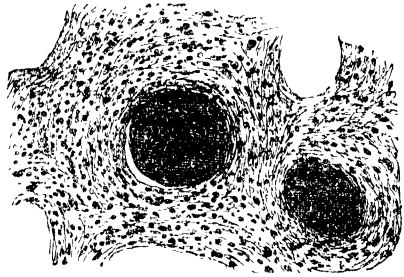
A, portion of a Yellow Tubercle from the Lung in a Case of Acute Tuberculosis.—Showing the degeneration of the central portions of the nodule *c*, and the cellular thickening of the alveolar walls and accumulations within the alveolar cavities at the periphery *p*. × 100.

the accumulations within the alveoli and the cellular infiltration of the alveolar walls are visible only at their periphery. This is always the case in the distinctly yellow tubercles. (Fig. 95.)

The histological characters of the firmer grey nodules differ somewhat from the preceding. In these the cellular infiltration and thickening of the alveolar wall is

much more marked, and many of the alveolar cavities are occupied by giant cells, these probably originating, as described by Dr. Klein, from the alveolar epithelium.* (Fig. 96.) In other cases, the alveolar structure has completely disappeared, and the tubercle, when examined with a low magnifying power, appears as a little somewhat spheroidal mass, the cellular elements of which are seen to be grouped around separate centres. (Fig. 97.) When more highly magnified, these centres are seen to correspond with the giant-cells already described, and the

FIG. 96.



A portion of the more external part of a Grey Tubercle from the Lung in a case of Acute Tuberculosis.—Showing the extensive infiltration and thickening of the alveolar walls, and the giant cells within the alveolar cavities. × 100.

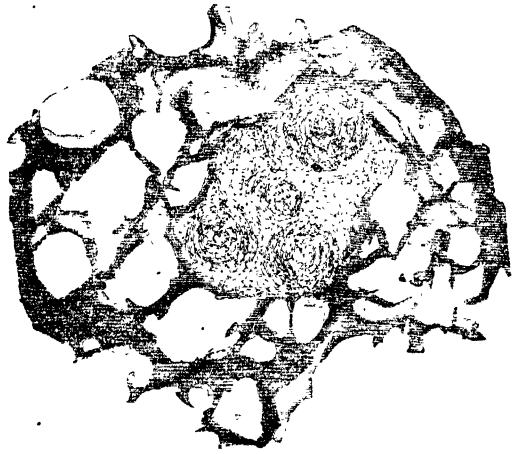
small-celled structure grouped around them, as is well shown in Fig. 86. This is a fully developed tubercle of the lung. The small-celled structure at the peripheral portions of the nodules extends into and produces a thickening of the walls of the alveoli with which the nodule is incorporated. (Fig. 98.) In the tubercles thus constituted, extensive

* These large multinucleated cells are stated by Dr. Klein (*loc. cit.*) to originate either by the fusion of the alveolar epithelium, or by the excessive development of one epithelial cell. Since the publication of Dr. Klein's statement I have frequently observed these cells situated distinctly in the alveolar cavities, and I have little doubt they originate in the way he describes.

retrogressive changes rarely occur. Degeneration is slow and very incomplete, and the nodule often becomes imperfectly fibroid.

Respecting the cause of these differences in the histological characters of the miliary lesions in the lungs—I believe them to depend upon differences in the age of the

FIG. 97.



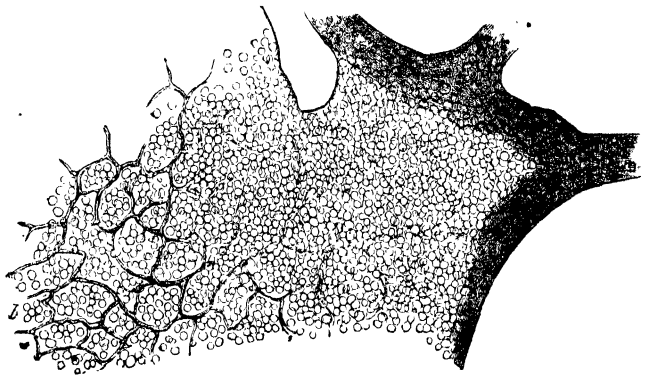
A firm Grey Tubercle from the Lung in a case of Acute Tuberculosis.—Showing the grouping of the elements around separate centres, the nodule consisting of several giant-cell systems. × 33.

nodules, and in the intensity of the tuberculous process.* If the intensity of the process be considerable, the nodules will consist in the main of accumulations of epithelium within the pulmonary alveoli, and the nodule will rapidly undergo disintegration. (See Fig. 95.) If the process be less intense, and the nodules attain a more advanced age, degeneration will be less rapid and complete, the cellular infiltration and thickening of the alveolar walls will be

* Intensity comprises two factors—severity of injury and susceptibility of injured tissue. (See "Inflammation.")

greater, and the epithelial elements may form large multinucleated cells. (See Fig. 96.) Lastly, in the least intense and most chronic processes, the development of multinucleated elements and the formation of the network of branched cells reaches its maximum (see Figs. 86

FIG. 98.



A small portion of the most external part of a firm Grey Tubercle from the Lung in a case of Acute Tuberculosis.— Showing the incorporation of the nodule with the alveolar wall *a*. × 270.

and 97), degeneration takes place slowly in the central portions of the nodule, and there is often considerable fibroid induration of the new tissue. There is thus a close analogy between the tissue changes resulting from tuberculosis of the lungs and those which result from other chronic inflammatory processes. (See "Chronic Inflammations.")

CHAPTER XXX.

THE INFECTIVE GRANULOMATA (*continued*).

LUPUS VULGARIS.

THIS disease is characterised by the appearance of nodules of granulation tissue upon the skin (chiefly of the face), and much more rarely upon the mucous membranes of the conjunctiva, pharynx, vulva and vagina. The tubercles are situate primarily in the corium, and may reach the size of a pea; fresh ones appear at the periphery, whilst those in the centre blend into a more or less diffuse infiltration. The disease appears almost always between the age of two years and puberty, and is especially common in the scrofulous.

Structure.—The nodules consist of granulation tissue containing epithelioid and often a good many giant-cells. They differ from true tubercles in being rather richly vascular. The intercellular substance is scanty and homogeneous. It is not uncommon to find that long anastomosing processes of epithelium have grown down into the round-celled growth, the physiological resistance of which would seem to be less than that of normal corium.

Course.—Spread occurs by the production of fresh nodules at the margin of the primary focus. The course is always chronic. When the patch has reached a certain size it may undergo no change for a long time; the nodules and infiltration may end in degeneration and **absorption**, a white scar being left, or in **ulceration.** After eating away the tissues to varying depths, sometimes destroying large portions of the nose, lip or eyelid, the ulcers may heal; or healing may go in at one point and destruction at another.

Etiology.—The mode of extension is indicative of spread of the cause by the lymphatics. The nature of this cause is

doubtful. Some believe that lupus is a local tuberculosis; the Bacillus tuberculosis has several times been found in the nodules, but very inconstantly. Tuberculosis has been produced by inoculation of lupus tubercles; but much more commonly it fails. The relation to scrofula must be noted. As above stated, lupus nodules are vascular, and rarely become caseous. Schüller found micrococci in the epithelioid cells.

GLANDERS AND FARCY.

THESE are varieties of one disease, due probably to difference in the point of entry of the poison. In Glanders, the nasal mucous membrane and its prolongation are the seat of the earliest lesions; in Farcy, the skin and sub-subcutaneous tissue. Each form may run a rapid or a slow course, and it is usual in man for the symptoms of one to supervene sooner or later upon those of the other. The diseases are common among equine animals, especially horses, and are communicable from them to other animals, including man. This happens but rarely. It is transferable from man to man.

Nature of the Pathological Lesion.—This is best seen in the more chronic forms. It is a circumscribed nodule (*farcy-bud*) varying from a just visible point up to the size of a pea or bean. On section it is found to consist of small round cells; vascularisation is very imperfect, if it occurs; but the formation of larger cell-forms has not been described. Degeneration occurs early, and more or less acute suppuration is excited. In the substance of an organ or part an abscess forms, but, on a free surface, an ulcer, with indurated, sharply cut margin and very foul base is the result. Such ulcers may heal, but their course is generally very chronic. In the more acute forms of the disease the poison sets up

ordinary suppuration at spots where it develops. The inflammation is not always circumscribed, but sometimes produces diffuse infiltrations—as of muscles, subcutaneous tissue, and connective tissue of orbit—which go on to suppuration at many points or generally. The farcy-buds and diffuse imflammations, in the various stages of degeneration, suppuration, and ulceration mentioned above, and in various seats, constitute the morbid anatomy of the disease.

Mode of Entry of the Poison.—A wound is a common portal; mucous membranes, especially the conjunctival and nasal, are other seats of infection. In many cases there is no evidence to show how the poison entered.

Course.—In acute glanders, after a variable period of incubation, inflammatory nodules appear in the mucous membrane of the nose, frontal sinuses, &c., and run on more or less rapidly to suppuration and ulceration. The submaxillary and cervical glands swell from infection through the lymphatics. The fever, and the muco-purulent, often bloody, discharge from the nostrils are thus explained. The poison now enters the blood and is carried to distant parts, giving rise to metastatic inflammations in internal organs, especially the lungs, and in the skin, and the mucous membranes of the respiratory and alimentary tracts. Abscesses in the subcutaneous and intermuscular tissue are common, and suppuration in joints occurs. In fact the disease resembles pyæmia in many respects, being like it due to the dissemination by the blood of a poison capable of exciting suppuration. The abscesses in organs are generally small, but may reach a large size. The respiratory and alimentary mucous membranes are perhaps directly infected from the nose. On the skin, red papules and larger patches of inflammation appear, on which vesicles, and then pustules, often with hæmorrhagic contents, quickly develop—constituting the rash of the disease. The earliest stage is a collection of round cells in the superficial part of a papilla; a little

later and the rete is raised in the roof of a pustule. Throughout the disease the fever is high, symptoms of prostration appear early, and death occurs with all the signs of septic poisoning.

In Chronic Farcy large "buds" appear in the subcutaneous, submucous, and intermuscular tissue. The former break down slowly and form foul ulcers, the lymphatics become much swollen, hard, and knotted; the glands are greatly enlarged. The general symptoms are much milder. This form often ends in recovery. The symptoms of glanders frequently supervene before death.

Etiology.—Schülz and Löffler* found in the pus of abscesses in glanders, slender rods, like, but smaller than, B. tuberculosis. Cultivated in the serum of horses' blood they formed colonies, maintaining their initial form. After repeated cultivation, to ensure purity from the original pus, different animals were inoculated. The result varied with their susceptibility. In all, an indurated ulcer appeared at the site of inoculation; and cordy lymphatics ran thence to swollen glands. In some, metastatic abscesses formed in internal organs; others died early, with symptoms of septic poisoning. In all, the above bacillus was found. Two horses were inoculated from a fourth cultivation: all the symptoms of glanders set in, after some days' incubation, and the older horse died in fourteen days. The other was killed next day, being extremely weak. The post-mortem signs were the same in both—viz., a sore the size of a shilling at the site of inoculation; lymphatics leading thence to glands, hard and swollen; abscesses in the lungs, from the size of a pea downwards, with red borders; the nasal mucosa studded with farcy buds and ulcers.

By this one series of experiments, it would seem that this bacillus has been proved to be the cause of Glanders and Farcy.

* "Mittheilungen aus d. Kaiserl. Gesundheitstunt," Berlin, vol. ii.

LEPROSY.

This disease is endemic in many parts of the world, especially in the East and West Indies, China, South America, and Equatorial and Southern Africa. Formerly it was widely spread over Europe, and still lingers at many spots, particularly in Norway and Sweden.

Nature of the Pathological Lesions.—There are two chief varieties of this disease—**tubercular** and **anæsthetic.** In the former the lesions affect chiefly the skin, in the latter the nerves.

In **tubercular** leprosy, patches of hyperæmia are followed by thickening of the skin and the formation of nodules, which may reach the size of walnuts. They are almost always situate on parts exposed to the air—face, hands and feet—and appear sometimes singly, sometimes in groups. They may come out in distinct eruptions, separated by long intervals of time. At first firm and red or brownish, they become soft and paler, but do not, as a rule, ulcerate for long periods, unless injured. When ulcers do form, they cause great destruction of features. Healing may occur. The tubercles may affect other parts of the body, especially the extensor aspects of limbs, and the mucous membranes of the eye, nose, mouth and larynx.

In **anæsthetic** leprosy, nodules, or, more often, diffuse cylindrical or fusiform swellings, form upon nerves, especially the ulnar and external popliteal, surrounding long portions of them, affecting primarily the cutaneous and later the muscular branches. The skin supplied is often painful and hyperæsthetic at first, and then becomes anæsthetic, pale, and wastes, together with the paralysed muscles. Ulcers form sooner or later upon the anæsthetic parts, leading to extensive destruction and dropping off of fingers, toes, and larger portions of limbs.

The two forms may run their course separately, but often occur together. The anæsthetic variety occurs chiefly in hot climates. In each form the glands receiving lymph from the diseased parts enlarge, first the superficial ones, then the deeper. Infiltration of viscera

—especially the liver, spleen and testes—may occur. To the naked eye, the new growths have the greyish or yellowish, semi-transparent, uniform appearance common to so many cellular structures. Microscopically, they consist of a granulation tissue: it is made up of small round cells, like leucocytes, and some very large ones—lepra-cells—of which some are spindle or branched. A few vessels lie among them. The appearances are well shown in the accompanying drawing, made from a specimen kindly lent by Dr. Thin (Fig. 99). As above stated, the tendency to degenerate is much less marked than in most allied growths.

FIG. 99.

Tubercular Leprosy.—Section through skin. *a*. Showing infiltration with leprosy bacilli. × 6. *b*. shows individual bacilli in the cells. × 300. *c*. Individual bacilli showing spores. × 800.

Etiology.—From time immemorial leprosy has been looked upon as a contagious disease, and lepers have been rigorously expelled from social communities. A very superficial examination throws doubt upon this; for many lepers live in the closest relations with healthy people without communicating the disease. Many have, however, maintained that the disease is communicable under certain conditions (among which susceptibility, perhaps, ranks high) which are rarely realized. Hillis* has brought forward evidence in favour of this view.

* "Leprosy in British Guiana."

According to modern views, endemicity at once excites suspicion that a disease is infective. Organisms have therefore been searched for in leprosy. Neisser* and Hansen† separately described a bacillus as specific to leprosy. It is found constantly in all young, primary lesions (not in those secondary to anæsthesia); chiefly in the lepra-cells (Fig. 99*b*), but also in others, rarely between cells. In old lesions they become granular from spore-formation. They show an active to-and-fro movement in fresh juices, and, when cultivated, grow into long jointed filaments (Hansen). Thin‡ has shown that as regards size, beaded appearance, and staining, B. lepræ (Fig. 99*c*) is exactly like B. tuberculosis. The organism is the same, no matter where the disease may have been contracted. Thin found bacilli in enormous numbers in the lesions he examined, and gave reasons for believing that spread may occur by both lymph- and blood-vessels; but the fungi have not been found free in the blood of patients. Neisser produced tubercles in dogs and rabbits by inoculation from leprosy lesions; Hansen failed with rabbits, and Köbner with an ape. The bacilli multiply in the anterior chamber of rabbits, but produce no tubercles.

ACTINOMYCOSIS.

The exact nature of the parasite found in actinomycosis or ray-fungus, and its botanical position, are not determined. It is believed by many to be the conidia-form of perhaps some known species.

Sarcoma-like tumours occurring chiefly in the lower jaws of cows were shown by Bollinger in 1877 to contain constantly elements of a fungus—the actinomyces—and he found the same fungus in nodular masses in the

* "Bresl. ärztl. Zeitschr.," Nos. 20, 21, 1879.
† "*Virchow's Archiv*," vol. xxix. p. 31.
‡ "Trans. Med. Chir. Soc.," 1883.

tongues of cows (woody tongue), in the swollen glands beneath the jaw, and in the upper part of the neck, in polypoid and submucous tumours of the larynx, and throughout the alimentary tract. They have since been demonstrated in tumours of pigs' jaws and udders; and in tubercle-like nodules in the lungs of calves. On section these nodules have a spongy, open appearance, and a puriform or cheesy fluid can be squeezed from them. Besides fatty cells, this contains many pale yellow granules, as large as millet-seeds. These, when gently squeezed and cleared up by potash, are seen to consist of filaments radiating from a common centre, and bearing at their free ends club-shaped swellings, often branched. The nodules and tumours consist largely of granulation tissue, intersected here and there by bands of fibrous tissue. In the older specimens there are found, round each fungus-collection, giant-cells, and outside these epithelioid and then granulation-cells—all signs of a chronic inflammation.

In 1878 Israel described a case of multiple superficial abscesses, and one large intra-thoracic abscess opening by fistulæ on the surface. The pus from all contained parasites which corresponded to the above description. The disease had begun six months before with fever and joint-pains. Three weeks after admission the woman died: there was a great abscess in the left lung, and countless abscesses in the liver, spleen, intestine and kidneys, most of them very small, but some the size of an apple. All contained the fungi, and in the glomeruli of the kidney were found fungi which had not yet excited inflammation. The point of entry of this fungus was not evident, but in pus from a tooth-socket in another case Israel found the same organism.

Some eighteen or twenty cases have now been described, and in several the disease began distinctly in the lower jaw, from a carious tooth, or after its extraction; in others the point of entry was obscure. All the cases were very chronic, and in many the disease spread only locally, burrowing

in all directions, and for long distances from its starting-point. In others, as in the above case, evidence of embolism was unmistakable. Secondary deposits have been found in all organs; and Ponfick has seen a granulation-tumour growing into the jugular, and in the same case there were growths in the right auricle and ventricle.

In man the fungus often spreads from the region of the jaw to the front of the cervical spine, producing a prevertebral abscess, or it excites inflammation in the region of the thoracic or lumbar spine, causing caries of the bones and wide-spread fistula-formation. As a rule the growths break down; but tumours like those in animals may be found.

CHAPTER XXXI.

SYPHILIS.

The lesions occurring in the course of constitutional syphilis also belong to the class of Infective Granulomata. They are inflammatory in their nature, but in their seats, distribution, sequence, and histological characters, many of them present certain pecularities which make them quite characteristic of this disease. The primary syphilitic lesion (usually the indurated chancre), the secondary lymphatic gland enlargement, and the subsequent series of changes in the skin, mucous membranes, and, later, in the nervous system, bones, and internal organs, are all of them the results of inflammatory processes, induced by the syphilitic poison.

Early Lesions.—Many of these are, anatomically, indistinguishable from simple inflammations of the same parts. The rashes, for example, are due to inflammatory hyperæmia with more or less infiltration of the superficial layer of the skin, enlargement of the papillæ, and, often, excessive epithelial multiplication. As a rule these in-

flammations end naturally in resolution; but in tissues of feeble resisting power they may ulcerate. The early periostitis (nodes), again, is indistinguishable from a traumatic inflammation, and the syphilitic iritis is diagnosed from the rheumatic only by concomitant circumstances.

Later Lesions.—Equally characteristic, clinically, with the above are the diffuse subacute and chronic inflammations of organs and parts which end in **fibroid induration.** But, anatomically, these are ordinary productive inflammations. Granulation tissue forms more or less irregularly throughout the organ. At the same time, if the process is subacute, degeneration and disappearance of some of the more or less widely separated elements of the part occur. Scar-tissue forms from the granulation tissue, and, as it contracts, many more of the proper cells of the part atrophy and disappear. The appearance of the infiltration varies in different cases and in different parts of the same organ—consisting now almost wholly of cells with little intercellular substance, or, again, of more or fewer cells in a markedly fibroid matrix, or, finally, of dense fibrous tissue. The infiltration may be general, but much more commonly comparatively healthy portions of the organ are found between the fibroid indurations. It is the irregular distribution of these lesions which makes them so characteristic of syphilis.

The capsules of organs are irregularly thickened; and peritoneal coverings are sure to be involved, producing more or less general adhesion to surrounding parts, as is seen in syphilitic hepatitis, splenitis, or orchitis. In the latter case, the coincidence of hydrocele proves during life the affection of the tunica vaginalis. The irregular thickening of the capsule is the most marked feature.

As the fibrous tissue contracts, the organ shrinks as a whole, and often becomes of stony hardness; but the irregular distribution of the exudation, above noted, often causes unequal contraction and puckering of the surface, amounting in some cases to the formation of deep fissures,

dividing the organ into lobes. In these cases the diffuse growth has probably been combined with the syphilitic tumour or gumma (to be next described), as not uncommonly happens.

Naked-eye examination of a part, *e.g.*, testis, which has undergone these changes, shows adhesions between the layers of the tunica vaginalis, which contains fluid where not adherent; marked thickening of the tunica albuginea and, extending from it into the organ towards the mediastinum, dense bands of fibrous tissue; the natural reddish-brown colour of the tubules is replaced by a much paler whitish-yellow tint, in which islands of normal tissue may remain. The consistence of the gland is greatly increased. One or two gummata may also be present.

In relation with bone, exudations of this kind often ossify. Under the periosteum, they cause thickening of the bone. In the Haversian canals and cancellous spaces increased density of it (see "Condensing Ostitis").

These cell-exudations do not always go on to fibroid induration; they may resolve, and generally do so with marvellous rapidity, under the influence of iodide of potassium when they are at all recent. Probably the inflammatory products undergo fatty degeneration previous to absorption.

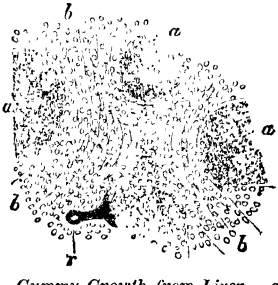
Localised scars often causing much puckering of the surface of organs, and sending fibrous rays far into the surrounding tissue may be found, and are usually the remnants of precedent gummata.

Gummata, Syphilitic Tumours, Syphilomata. — Anatomically these are the characteristic lesions of syphilis; they are frequently associated with the fibroid lesions. As usually met with they are moderately firm yellowish-white nodules, having often, on section, somewhat the appearance of the cut surface of a horse-chestnut. They vary in size from a hemp-seed to a walnut, and are surrounded by a zone of translucent fibrous-looking tissue, which sometimes has the appearance of a capsule,

and which is so intimately associated with the surrounding structures that enucleation of the mass is impossible. The outline of the growth is generally irregular from processes radiating from it along the natural septa of the organ, and examination always shows that spread occurs by infiltration. In the earlier stages of their development, when they less commonly come under observation, they are much softer in consistence, more vascular, and of a reddish-white colour; whilst in their more advanced stages, owing to extensive retrogressive changes, they may be distinctly caseous.

Examined microscopically, gummata, as usually found, show marked structural differences between the central and external portions of the growth. The central portions are composed of closely packed shrunken cells and nuclei, fat granules, and cholesterin, amongst which is generally a little fibrillated tissue. (Fig. 100 *a*.) Surrounding this and directly continuous with it is a zone of cells in a distinctly fibrillated matrix; whilst the peripheral portion of the growth is a richly cellular and vascular tissue. (Fig. 100 *b*, and Fig. 101.) This peripheral layer, which is in direct histological continuity with the surrounding structures, consists of small cells, many of which resemble white blood-corpuscles, whilst others are larger and like the formative cells of granulation tissue; giant-cells also are found, but less commonly than in tubercle. These cells are separated by a scanty, homogeneous, intercellular material and numerous new blood-vessels. The three zones already described, which are to be

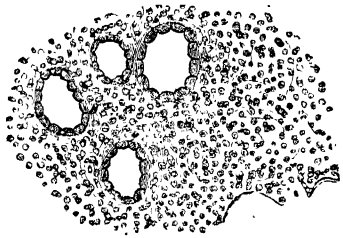
FIG. 100.



Gummy Growth from Liver.—*a*. Central portions of growth consisting of granular débris. *b*. Peripheral granulation tissue. *r*. A bloodvessel. × 100. (Cornil and Ranvier.)

distinguished more or less clearly in most fully developed gummy nodules, correspond with three different stages in their growth. Caseation may follow very closely on the spreading edge and render the two outer zones very narrow; although to the naked eye the caseous patch may seem defined, the microscope shows that each one of these zones passes gradually into the next. The most external zone, consisting of the vascular granulation tissue, represents the earlier stage of development, and by the continuous formation of this tissue the growth may steadily increase. The intermediate more fibrous zone represents the second stage in the process—the development of the granulation tissue into a more or less completely fibrillated structure. The character of this fibrillated

FIG. 101.



The Peripheral Portion of a Gummy Growth in the Kidney.—Showing the small-celled granulation growth in the intertubular tissue. × 200.

tissue vary in different growths. In some the fibrillation is very distinct; in others, the tissue is dense and cicatricial in character; whilst, less frequently, it consists of a reticulated structure within the meshes of which are grouped round small cells. The central zone, consisting of the amorphous granular material, represents the oldest portion of the growth—that which has undergone retrogressive changes. The blood-vessels in the centre of a gumma undergo certain changes, about

to be described, by which they become obliterated. The parts are thus deprived of blood and hence degenerate. This takes place very early. When the tumour is large, it may sometimes be seen to be made up of several distinct smaller growths, each presenting at its circumference the more perfect cells, whilst its central parts are granular and amorphous.

In early stages, before they have produced marked ...ruction of tissue, gummata may be absorbed. Later, ... central fatty portions are frequently absorbed, leav- ... radiating puckered scar (p. 331); calcification is rare. Not uncommonly, under conditions which are not understood, gummata soften and excite suppuration around them; the abscess bursts, and a yellow slough is exposed. This has a very characteristic appearance, like "wet wash-leather." Slowly it is thrown off, and a larger or smaller cavity is left, with ragged soft margins. All this is often and well seen in the tongue. Gummata of the skin and mucous membranes are by far the most prone to take this course. These ulcerations must be distinguished from the superficial ulcerations connected with the early rashes.

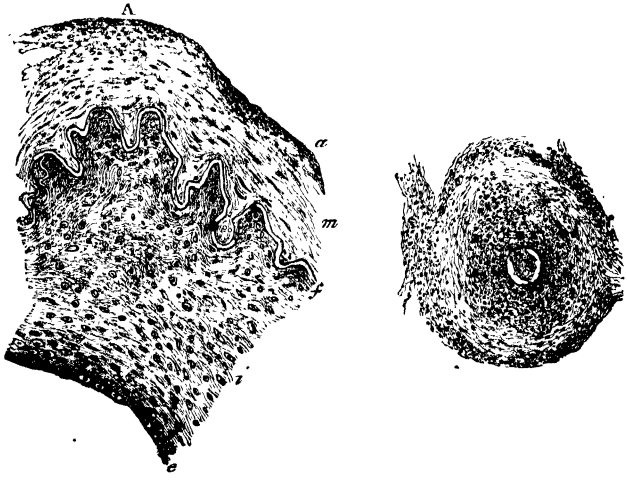
Gummata are met with in the skin and subcutaneous cellular tissue; in the submucous tissue, especially of the pharynx, soft palate, tongue, and larynx; in muscle, fasciæ, bone; and in the connective tissue of organs—especially of the liver, brain, testicle, and kidney. They occur also, but much less frequently, in the lungs; as do also simple localised fibroid indurations. They are generally late, so called tertiary, manifestations; but they may occur at quite an early stage. No hard line can be drawn clinically between the secondary and tertiary stages, and none can be drawn pathologically between the products of these stages. All are inflammatory, some circumscribed, some diffuse. Even the hard chancre has the structure of the first stage of a gumma—leucocytes, formative and giant-cells in a fibrillar matrix.

Changes in Vessels.—Certain changes in the cerebral arteries have been described by Heubner as charac-

teristic of syphilis. These changes have been brought prominently before English pathologists by Drs. Greenfield, Barlow, and others.*

In the cerebral arteries the changes produce opacity and marked thickening of the vessel, with considerable

FIG. 102.



Syphilitic Disease of Cerebral Arteries.

A. Segment of middle cerebral artery, transverse section—*i*, thickened inner coat; *e*, endothelium; *f*, membrana fenestrata; *m*, muscular coat; *a*, adventitia. × 200 reduced ½.

B. Small artery of pia mater, transverse section.—Showing thickened inner coat, diminished lumen of vessel, and considerable infiltration of adventitia. The cavity of the vessel is occupied by a clot (? thrombus). × 100, reduced ½.

diminution in its calibre. It is this diminution of the lumen of the vessel which is especially characteristic.

* "Trans. Path. Soc. Lond.," vol. xxviii.—*Visceral Syphilis.*

The smaller vessels, arteries and veins, are chiefly affected, and their lumina may be quite obliterated.

When transverse sections of the vessels are examined microscopically, the principal change is seen to be situated in the *inner* coat. It is well shown in the accompanying drawings made from specimens kindly lent to me by Dr. Barlow. (Fig. 102.) This coat is considerably thickened by a cellular growth. The growth, which is limited internally by the endothelium of the vessel (Fig. 102A, *e*), and externally by the membrana fenestrata (Fig. 102A, *f*), closely resembles ordinary granulation tissue, consisting of numerous small round and spindle-shaped cells. This tissue appears gradually to undergo partial development into an imperfectly fibrillated structure.

In addition to this change in the intima, the outer coat is abnormally vascular and infiltrated with small cells (Fig. 102A, *a*), and this cellular infiltration usually invades also the muscular layer (Fig. 102A, *m*). The marked diminution of the lumen of the vessel (Fig. 102B), and the consequent interference with the circulation, coupled with change in the endothelium, frequently leads to coagulation of the blood (thrombosis) and cerebral softening.

Dr. Greenfield's observations tend to show that similar changes occur in vessels of other parts, and that they account for the degeneration of syphilitic gummata. Aneurism in adults under forty is often connected with a syphilitic history.

Etiology.—Strong as the clinical evidence of the infective nature of syphilis is, nothing positive is known of its cause. The observations on this subject are few.

Klebs described mobile granules and short rods in non-ulcerated primary sores. He inoculated apes with portions of syphilitic tissue, and produced a disease closely resembling syphilis. A cultivation of the blood of such an ape on gelatine yielded brownish masses of short rods, as does also the primary lesion in man.* Aufrecht found

* "Arch. f. Exp. Path." x. 3-4.

diplococci staining with fuchsin in the juice of flat emdylomata.* Birch-Hirschfeld found diplococci, which are easily taken for short rods, not only in the papillary bodies and epidermic cells of flat condylomata, but also in gummata of different organs, but only in still-growing specimens, and especially at the edge of the cheesy part. Bergmann found organisms resembling those described by Klebs constantly present in the lymphatics of Hunterian chancres.† Martineau and Hamonic cultivated in meat broth similar organisms from the discharge of syphilitic ulcers; the cocci grew into larger chains, and, the authors say, gave syphilis to a young pig.‡

The poison exists in the primary sore, in mucous tubercles, and all secondary sores, and in the blood during the eruptive period. It is doubtful whether it is present in pure lymph, such as may be obtained from a vaccine-vesicle. It is not present in normal secretions, as saliva, mucus, semen. The discharge from tertiary or gummatous ulcers is not infective, but this would by no means disprove Birch-Hirschfeld's observations on gummata.

SYPHILITIC DISEASE OF THE LIVER.

The liver is one of the most frequent seats of syphilitic lesions. The most common change is the development of fibroid and gummy growths in the substance of the organ. In the spreading stage the margins of gummata are ill-defined, round cells infiltrating the surrounding liver-tissue. The growths — which are usually connected with fibroid thickenings of the capsule — sometimes consist simply of a dense fibroid structure. More commonly, however, gummy masses are found imbedded in the fibroid growth. In the former case it is possible that the gummy mass may have become absorbed, leaving merely its fibroid cicatrix.

The development of these growths produces very

* "Cebl. f. Med. Wiss." p. 228, 1881.
† The Fungus of Syphilis.
‡ Birch-Hirschfeld, "Lehrbuch d. Path. Anat." p. 187, 2nd edit.

marked alterations in the form of the liver. Scar-like depressions are seen on its surface, and the organ is irregularly and often very deeply puckered.

A more general fibroid change, not associated with the formation of gummy masses, is occasionally met with in the liver in inherited syphilis. This change closely resembles ordinary cirrhosis, although the intercellular network of the liver is usually more extensively involved.

Lastly, it must be mentioned that the liver in syphilis is frequently lardaceous.

It is unnecessary to describe particularly syphilitic lesions in other organs, as they all present the same general characters—viz., scars, fibroid indurations, and gummy growths, singly or combined.

CHAPTER XXXII.

SCROFULA.

THE constitutional condition known as Scrofula is characterised by a liability of certain tissues to become the seat of chronic inflammations, the causes of such inflammations being very slight and sometimes wholly hypothetical. It is generally believed that these tissues either possess congenitally, or acquire as a result of abnormal conditions of life, an enfeebled resisting power against injury. Virchow says their **vulnerability** is excessive. Consequently, the above slight or undiscoverable causes, injuries which would have no effect or only the most passing upon a healthy subject, produce inflammation in the scrofulous. In this way it is sought to account for the **abnormal susceptibility to inflammation.**

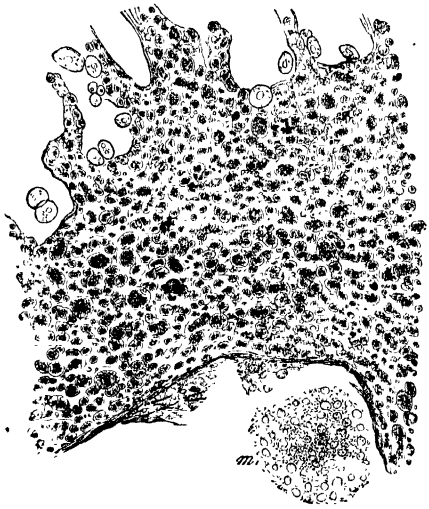
The explanation given of the **abnormal chronicity** of the processes is very similar. We know that chronic inflammation implies the prolonged or frequent action of a cause. It is almost impossible to put an inflamed part under such conditions that no cause of inflammation, as friction, pressure, tension, &c., can affect it. These are not sufficient to keep up an inflammation in a healthy person, but in the vulnerable tissues of the scrofulous they are supposed to be able to do so; and doubtless they aid in rendering the process chronic.

This susceptibility, although more or less general, is commonly most marked in the mucous membranes and in the lymphatic glands, especially in those glands which stand in direct relation with the fauces, tonsils, and pharynx (cervical); with the lungs (bronchial); and with the intestine (mesenteric). It is to these, it may be remarked, that organisms are most likely to obtain access. The skin (eczema impetiginodes), bones, and joints (caries, caries necrotica, and chronic arthritis) are also liable to be affected. The part which suffers varies in different cases, and injury is often the determining cause.

With regard to the tissue-changes occurring in scrofulous inflammation—it must remembered that when inflammation occurs in a healthy individual, if it does not cause the death of the part, the inflammatory products either become absorbed, or the process leads to suppuration, or to the formation of a vascularised connective tissue. In scrofulous inflammation the absorption of the inflammatory products is very much less readily effected; they tend to **infiltrate** and **accumulate** in the tissue, where by their pressure they interfere with the circulation, and so lead to retrogressive and **caseous** changes. There is but little or no tendency to the development of new blood-vessels, and hence there is no organisation of the new growth. These peculiarities are to be in great measure ascribed to that inherent low vitality of the tissues which obtains in this disease,

and also to certain peculiarities in the histology of the inflammatory products. Virchow long ago pointed out the richly cellular character of the products of scrofulous inflammation, the tendency of the cells to infiltrate the tissue, and the extreme tardiness with which the infiltra-

FIG. 103.



Scrofulous Inflammation of a Bronchus.—Section of a small bronchus of a markedly scrofulous child, the subject of bronchitis, which terminated in miliary tuberculosis. The deeper structures of the bronchial wall are seen to be extensively infiltrated with cells, most of which are *larger* than those met with in the less extensive infiltration of healthy inflammation. The infiltration extends to and invades the walls of the adjacent alveoli, which are seen at the upper part of the drawing. The cavity of the bronchus contains a little mucus, *m*. × 200, reduced ½.

tion becomes absorbed. Rindfleisch stated that these cells are, for the most part, **larger** than those met with in healthy inflammations; and that this being the case,

their removal by passage into the lymphatics is less readily effected. Giant-cells also are very constantly met with. There is probably, however, no difference between these elements and the formative and giant-cells which Ziegler found in all chronic inflammations (p. 276). This large size of many of the young cells in scrofulous inflammation, and their marked tendency to infiltrate and accumulate is well shown in the accompanying drawing (Fig. 103).

We now come to a question which has long been a subject of discussion, and which is of great importance in the etiology of scrofula—viz., its **relation to tubercle.** It is generally held, and probably rightly so, that scrofula favours tuberculosis; and clinically we know that tuberculous processes are especially prone to occur in the scrofulous. The similarity in the histology of the lesions, however, together with the fact that the Bacillus tuberculosis is often found in what appear to be simply scrofulous products, has suggested the possibility that the two diseases are identical—that the peculiarities of scrofulous inflammation are also due to the presence of the specific bacillus, and not simply to an inherited or acquired abnormal susceptibility to simple injuries. This view receives some support from a consideration of the ready union obtained in amputations for strumous disease, the good results of *complete* excision of diseased synovial membranes, and of enucleation of strumous glands, which would seem to show that extremely severe injuries may be inflicted upon the tissues of strumous patients, and that they may subsequently be exposed to those minor injuries, and even to the irritation of septic discharges, which are held to render the inflammation chronic, but still they do not in the majority of cases become again the seats of intractable inflammation. It may be said that all the excessively vulnerable tissues of a part have been removed by amputation; but this can hardly be maintained in excisions in which parts of epiphyses are left, or in gouging operations upon

bones. The true explanation would seem to be that in all these cases we have removed not only the products of the inflammation but its cause; and what we know already of the etiology of chronic inflammation leads us to suspect the infective nature of the latter.

On the other hand, it may be said that in such cases as the above a scrofulous inflammation had already become infected with the tubercle bacillus; and when we remember the extreme frequency with which the mucous membranes and lymphatic glands in scrofulous children are the seats of obstinate and protracted inflammations which ultimately terminate in complete recovery, we cannot but question the identity of a scrofulous with a tuberculous process. It would seem more in accordance with the present position of our knowledge still to regard a scrofulous lesion as a simple but chronic inflammation, and a tuberculous one as specific and due to the Bacillus tuberculosis; the former constituting the soil which is most suitable for the development of this organism.

CHAPTER XXXIII.

INFLAMMATION OF SPECIAL TISSUES AND ORGANS.

THERE is nothing more to state concerning the process of inflammation, wherever it may occur. Every tissue in the body may be inflamed; but whilst this is common in some, it is rare in others. Certain forms of inflammation occur with especial frequency in certain parts; and the same part may present different appearances under the same form of inflammation. To these and similar points attention must now be directed.

The student should have quite ready in his mind the different forms of inflammation, and their names should bring before him a picture of the tissues infiltrated by a certain exudation; the possible fates of each exudation—complete absorption, imperfect absorption and its consequences, or death—must also be felt instinctively.

INFLAMMATION OF THE CONNECTIVE TISSUES.

Common connective tissue accompanies blood-vessels everywhere. When vessels are injured this tissue is more likely than any other to share in that injury; and if the vessels alone are damaged, it will be the first structure to experience the effects of the lesion. Thus, every form of inflammation occurs in connective tissue; the whole description of the process applies to it.

With regard to the special varieties of connective tissue, we shall speak first of the **non-vascular—cornea** and **cartilage**, both of which are interesting as the battle-grounds upon which the origin of the new cells in inflammation have been fought out; for it was hoped that migration from vessels would here be done away with. But we already know from Senftleben's experiments (p. 267) that injury of the cornea produces none of the anatomical signs of inflammation unless the marginal vessels are affected, or leucocytes are admitted from the conjunctival sac. About the third day, however, after destruction of cells regenerative processes set in. Observations on cartilage are more difficult, but they show that the above results hold good.

INFLAMMATION OF THE CORNEA.

Anteriorly and posteriorly the cornea is limited by membranes sufficiently stout to resist the passage of leucocytes, but these enter freely from the margin, together,

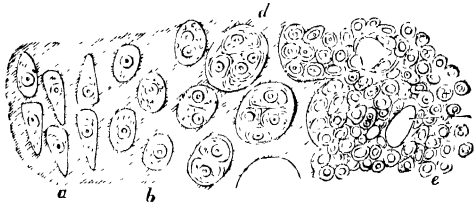
doubtless, with fluid exudation from the vessels, along the lymph-channels in which the cells and nerves lie, the leucocytes accumulating in clusters around the cells. Such exudation is accompanied by softening and opacity of the corneal structure, and may lead to alteration in its curvature. This happens in vascular keratitis and the interstitial inflammation of congenital syphilis. A slight vascular exudation forms beneath the roughened epithelium as a consequence of the irritation of granular lids, the condition being known as pannus. Pus may form between the layers of the cornea, constituting onyx; and ulcers in all stages are common. They heal by scar-tissue, and leave an opacity, and a more or less altered corneal curve. Any keratitis may be "productive," and result in opacity and altered curve.

INFLAMMATION OF CARTILAGE.

In the most acute inflammations of joints, the cartilage may slough bodily, as the cornea does in the worst cases of conjunctivitis, from injury and lack of food combined. It then either peels off in flakes or softens and wears away at points of pressure. In less acute cases it may be invaded by leucocytes from the joint cavity or from the bone. In the former case some white corpuscles may penetrate the injured part from the synovia; but the usual course is, that the synovial membrane becomes thickened by a vascular round-celled infiltration and sends processes inwards over the surface of the cartilage; these creep on, adhering like ivy, and their cells penetrate into the substance of the cartilage, eroding it. Primarily, or secondarily to this process, the subjacent bone may inflame, and granulation tissue springing from it may similarly eat its way through the cartilages at several points, riddling it; or it may spread out beneath its cartilage without perforating it, but loosening it so that it may fall into the joint-cavity. As a rule, no sign of multiplication of cartilage cells is seen, although leucocytes

naturally collect in their capsules (Fig. 104); but regenerative changes probably occur in chronic cases. In such a joint the fluid is always turbid from degenerating leucocytes and their products—thus differing from that of serous synovitis; the transition to pus is easy, with more intense irritation. Healing takes place by the formation of scar-tissue from the round-celled exudation; short, extremely strong and wide adhesions bind the surfaces together producing fibrous ankylosis. If the bone is involved some or all of the adhesions will ossify—bony ankylosis.

FIG. 104.



Section of Inflamed Cartilage.—*a.* The normal cartilage-cells. *b.* The same enlarged. *d.* Multiplication of cells within their capsules (probably invasion by leucocytes). *e.* Eroding layer of granulation tissue. × 250. (Cornil and Ranvier).

INFLAMMATION OF BONE.

Inflammation of bone always originates in its vascular structures—the periosteum and medulla. It is usual, however, to speak of an **ostitis** when the medulla lying in Haversian canals or cancellous spaces is affected; of a **myelitis,** when the medulla in the canal of a long bone is most markedly involved. Strict limitation of inflammation to one of these parts does not occur; hence such a term as osteo-myelitis.

PERIOSTITIS.—A **serous** form is described. It is rare, and is the mildest form of infective inflammation of the part. The exudation is highly albuminous (ostéite albuminense, Ollier).

Fibrinous and **productive** inflammations are common as the result of injury and syphilis. The early syphilitic node consists of granulation tissue which may be absorbed or go on to the production of fibrous tissue, which may ossify. It very rarely breaks down. Ossification begins beneath the periosteum, and from the surface of the bone. The vessels entering the Haversian canals in the latter are, on account of the elevation of the periosteum, more or less vertical to the surface; hence the new Haversian canals have the same direction. At first well-defined and easily separable from the old, the new and the old ultimately become indistinguishably blended. Later in syphilis, when gummata form beneath the periosteum, it is common for suppuration and superficial caries to occur. The subcutaneous bones are chiefly affected. Inflammatory thickening of a bone is always due to periostitis.

Suppurative periostitis is generally a part of the infective disease known as **acute necrosis,** which rarely, if ever, occurs after union of the epiphyses. It is believed by some that the poison lodges in the medulla, excites suppuration here, and spreads through Haversian canals to the periosteum to set up the same process; but probably it may affect the periosteum primarily and alone. Pus forming beneath this membrane strips it up over a larger or smaller area; the vessels passing into the bone are greatly stretched, and this together with the primary damage to the vessels induces thrombosis of many. Hence superficial necrosis is the usual result; and if the medulla also has suppurated, the necrosis will be total—involve the whole thickness of the shaft. Pyæmia commonly occurs before the abscess is opened; it is in this disease that infective fat-embolism probably occurs. In **septic osteo-myelitis** a diffuse suppurative inflammation attacks the medulla and periosteum, causing total necrosis of large portions of bone, and very frequently destroying the patient by pyæmia.

OSTITIS.—The mildest form described is that in which

granulation tissue is produced. This occurs much oftener in cancellous (vertebræ, tarsus, carpus, epiphyses of long bones) than in compact bone. A round-celled infiltration takes place in the medulla and presses into the Haversian canals; the fat cells disappear before it. So also does the hard substance of the bone; cancellous plates are eaten through and Haversian canals widen. A section shows the spaces crowded with small round cells, often developing in parts into fibrous tissue, and on the surface of the bone in contact with them are seen semilunar erosions as if small bites had been taken out of it. These are called Howship's lacunæ. Each contains leucocytes, formative cells, and often a giant-cell. These cells are eating away the bone. The normal bone-corpuscles remain unchanged so long as they are distinguishable. This process is called **rarefying ostitis**, and is an ulceration or **caries** of bone without formation of pus. Nothing is more natural than that a bone thus weakened should yield to pressure; thus bodies of vertebræ may disappear more or less completely, those above and below becoming approximated; and shafts of long bones bend markedly as is seen in ostitis deformans (Paget) and other diffuse inflammations. The inflammatory tissue may pursue any of the courses mentioned on p. 286.

In a very early case absorption might occur, and regeneration make good any loss. But when once marked destruction of bone has occurred, scar-tissue must form and ossify if a cure is to be effected, and this is what happens in cases of spinal curvature without abscess. Too often, however, degeneration and softening of the cells, with more or less suppuration occurs, a **cold abscess** resulting (p. 278). When this is opened the ulcerating, **carious,** surface of bone is exposed. If healing occur, it is by the development of healthy granulation tissue and subsequent scar-tissue, which ossifies. Tubercles are almost always found in such carious processes. Syphilis is another cause.

Breaking down of granulation tissue from closure of its vessels leads to death of the attacked bone; the pieces

which come away are generally of small size—**caries necrotica.**

In the most chronic forms of ostitis no rarefaction of bone occurs; the new growth slowly ossifies, and the Haversian canals and cancellous spaces diminish. The bone consequently becomes extremely heavy and ivory like; it is generally thickened irregularly from coincident periostitis. This occurs especially in the long bones and in the bones of the skull, from syphilis. It is called **condensing ostitis** or **sclerosis.** It is said that simple closure of a large number of Haversian canals may lead to death of the affected bone. In syphilitic necrosis of the skull the sequestrum is often very dense; it has probably been killed by degeneration and death of the inflammatory products in the bone around the sclerosed patch, and consequent destruction of the few vessels which entered it.

Nothing is commoner than to find the rarefying and condensing ostitis combined. Around carious patches, osteoplastic periostitis and condensing ostitis frequently exist, thickening and rendering more dense the surrounding bone. It may be that this less acute inflammatory process is coupled with true hyperplasia of the bony tissue.

NECROSIS.—We have already seen that death of bone may result in several ways from different forms of inflammation, each leading, however, to destruction of vessels and arrest of nutrition.

This may be brought about by injury stripping off the periosteum and breaking up the medulla; but the extreme rarity of necrosis, even in the most serious simple fracture, shows that injury alone, with the inflammation which it excites, is scarcely to be regarded as a cause. But it may act indirectly by preparing the nidus for septic (in compound fractures) and infective organisms. These constantly acting and severe irritants increase the damage so much that more or less extensive thrombosis, with death of the parts, ensues.

Suppuration beneath the periosteum and in the medulla are *the* causes of necrosis. This result is much commoner

in compact than in cancellous tissue, owing to the greater ease with which exudations compress the vessels in the unyielding channels of the former. Necrosis may occur also in a less violent way in rarefying and condensing ostitis (see *antea*), by death of the infiltration.

The piece of dead bone is called a sequestrum; it is cast off by a process of caries described on p. 348. It may be **total,** involving the whole thickness; **superficial,** or **central**—the latter being much the rarer.

The removal of the sequestrum from the granulation tissue with which it is in contact is often effected only with considerable difficulty, especially if it be deeply seated. This difficulty is occasionally due to a more or less thick layer of the old bone surrounding the necrosed portion. Much more frequently, however, it is owing to the participation of the periosteum in the inflammatory process. The inflamed periosteum produces new bone, a capsule of which is thus formed, inclosing the sequestrum. Openings exist in this capsule (*cloacæ*) leading to the dead bone, and through these openings the inflammatory products are discharged. When the sequestrum is quite superficial, its removal is, of course, more readily effected.

There are two other morbid conditions of bone, which although probably not coming within the category of inflammation, may be conveniently described in the present chapter—viz., **Mollities Ossium** and **Rickets.**

MOLLITIES OSSIUM.

Mollities Ossium or Osteomalacia is a rare disease, occuring only in adults, and especially in pregnant women who have borne many children. It is characterised by progressive decalcification of the bones, whilst the marrow increases steadily and becomes converted into a vascular round-celled structure. All bone is gradually absorbed, except a thin layer beneath the periosteum; so the bones

become mere shells in extreme cases, very light, easily cut with a knife, bending or breaking readily. Early in the disease fractures unite. On section in early stages the cancelli and Haversian canals are enlarged and full of a reddish, gelatinous substance, which at a later period may become yellow and fatty.

The nature of the disease is obscure. Sporadic cases occur everywhere, but it is frequent in some places; as in certain valleys about the Rhine, where, it is stated, there are women living who have undergone Cæsarean section for deformed pelvis more than once. The pelvic deformity is of chief importance; the sacrum is pushed downwards by the weight of the body, and the acetabula upwards and inwards by the resistance of the femora, thus greatly shortening the two oblique diameters.

Lactic acid has been found in the bone, the reaction of which is said to be acid, and in the urine. The latter usually contains excess of lime salts which have been removed from the bone and eliminated.

RICKETS.

This disease of children is so specially frequent in the large towns of England that it has acquired on the Continent the name of the "English disease." It appears to be caused by defective hygienic conditions, especially bad air and improper feeding. It is particularly common in children brought up by hand, and, according to Sir W. Jenner, becomes more severe in the later children of poor families. It may probably be said that all conditions which materially interfere with the nutrition of a child may cause rickets; and among these the absence of *fresh* food ranks highest.

The disease is characterised mainly by changes affecting the growing tissues of bones, and therefore most marked where growth is most active—viz., at the epiphyses of long, and at the margins of, flat bones.

These changes produce undue softness and consequent bending or breaking (green-stick fracture). The bone lesions are accompanied by symptoms of general ill-health, and often by enlargement of the liver, spleen, and less often, of the kidneys and lymphatic glands, due chiefly to increase of their interstitial connective tissue, but in part also to overgrowth of their essential structure (Dickinson).

The alteration in the bones may be briefly described as consisting in "an increased preparation for ossification, but an incomplete performance of the process" (Jenner). If we look at the end of a healthy, growing, long bone we see the white epiphyseal cartilage adherent along a straight line to the shaft which consists here of loose cancellous tissue, the spaces of which are filled with red marrow. Between the bone and the epiphysis is a blue, semi-translucent band about one millimetre broad with practically straight margins. Microscopically, the blue line is found to consist of the one or two layers of cartilage-cells which normally multiply and enlarge, forming the well-known oval groups among which ossification proceeds. The septa between these groups have become very thin, and towards the shaft they are calcifying; a sudden transition from the cartilage-cells to those of the vascular red marrow is seen. So soon as these spaces (primary areolæ) with calcified walls are occupied by the round-celled marrow, absorption begins, and adjacent spaces open into each other and form the larger secondary areolæ. On the walls of these laminæ of bone are deposited, including osteoblasts in lacunæ between them; and thus Haversian systems are gradually developed. The calcified cartilage-matrix is darker and more granular than the bone laid down by the medulla which gradually replaces it

In a ricketty bone, the blue transition zone is in its elements like that in health, but is much wider than normal, affecting several rows of cells, and its outlines towards the bone and towards the cartilage are very irregular, the calcification of the matrix to form primary

areolæ occurs without any regularity, so that patches of calcification or of young bone may be found in the transition-zone detached from the shaft, and oval collections of cartilage-cells are seen among secondary areolæ full of red marrow. Speedy fusion of the primary into secondary areolæ occurs, but the deposit of laminæ of bone is insignificant.

Beneath the periosteum, osteoblasts form in excess of the normal, and osteogenic fibres appear, but calcification is very backward. Central absorption goes on as usual to form the medullary cavity, and the sound bone which was laid down before the onset of the disease, and which was distinguished from the ricketty bone by its greater density and less opaque aspect, is gradually removed. The bone, now consisting only of the soft ricketty structure, yields more or less readily under pressure, or breaks under slight violence. The fracture, however, is often incomplete. When bending occurs, Nature endeavours to support the concave side by throwing out along it a buttress of bone. This is often seen in the femur and tibia, giving the bones a flat, somewhat razor-like appearance.

The thickening of the epiphyses, the displacements which occur about the junction of shaft with epiphysis, the thickenings of the edges of the cranial bones, as the parietals, and the abnormal curvatures of bones under pressure, are readily explained by conditions such as the above.

The process above described seems to be injurious to the subsequent growth of the epiphyses. They often join the shafts early, dwarfed stature being the result. We may just mention on account of its importance the ricketty pelvis. There are two forms. The first shows shortening of the conjugate diameter only, and is contracted in cases in which the child, being unable to walk, is kept lying. The other closely resembles the osteomalacic pelvis, and the mechanism of its production is the same, for it occurs in children who are able to walk about.

CHAPTER XXXIV.

INFLAMMATION OF BLOOD-VESSELS.

INFLAMMATION OF ARTERIES.

In studying the process of inflammation in arteries, it must be borne in mind that the middle and inner coats of these vessels are non-vascular, the bloodvessels being distributed in the external layers. As in other tissues, inflammation of arteries may be acute or chronic.

ACUTE ARTERITIS.—Acute idiopathic arteritis was formerly regarded as common, the staining of the inner coat which occurs in septic fevers being mistaken for inflammatory hyperæmia. No such disease is now recognised. Acute inflammation may be produced by **injury**, as when a vessel is tied, twisted, &c.; or by the formation or impaction in the vessel of an irritant body (**thrombus** or **embolus**); or by **extension** from surrounding parts. The changes in traumatic arteritis are described at p. 234, and the effects produced by a simple thrombus are similar. Plugging of an artery by a simple embolus causes only a chronic inflammation; but the infective emboli in cases of ulcerative endocarditis, &c., are believed to produce acute infiltration and softening, and to be the chief cause of aneurism in young people. In arteritis by extension the outer coat is first and chiefly affected; if the process extends so as to affect the intima, the endothelium becomes shed, and thrombosis results. Thus destruction of vessels by ulceration does not cause hæmorrhage, unless the clot breaks down, as it possibly will if infected from a foul wound. This is the commonest cause of secondary hæmorrhage.

CHRONIC ENDARTERITIS.—Whilst the acute inflammations affect more or less generally the whole thickness of the artery, the chronic inflammations affect

primarily and perhaps solely the deeper layers of the intima. Hence the term **chronic endarteritis.**

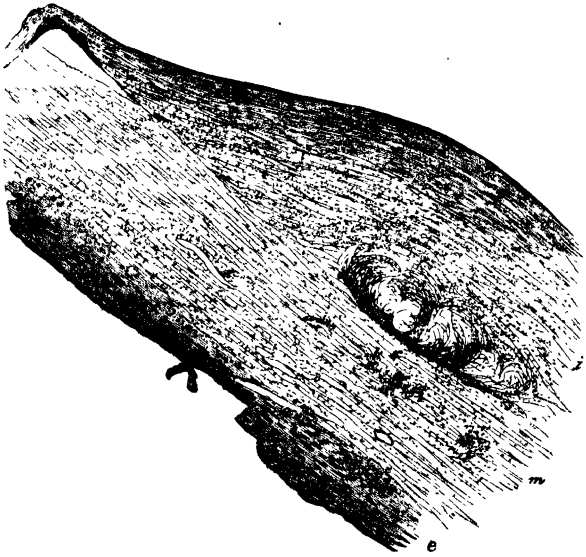
The **causes** of chronic endarteritis are **mechanical strain** and **syphilis.** The former has been shown by Moxon to be the cause of those very common changes in the larger arteries after middle life which go by the names—**chronic endarteritis, arteritis deformans,** or **atheroma.** The proofs adduced are—the much greater frequency of these changes in the aortic than in the pulmonary system; their occurrence in the latter when the pressure is raised, as in mitral obstruction; their relative frequency in those systemic arteries which are most exposed to strain, especially the arch of the aorta; and the effect of conditions which raise the blood-pressure in producing them. Thus athletes are very liable to the disease; and chronic Bright's disease, in which the high-tension pulse is well known, is a common cause of atheroma. **Syphilis,** as a cause of endarteritis, has been considered in a preceding chapter (see p. 335).

Atheroma affects chiefly the larger vessels of the trunk and limbs, and those at the base of the brain. It commonly forms rings round the mouths of branches leaving a main trunk. It appears as slightly prominent yellowish patches, covered by normal endothelium; in fact, this and the superficial layers of the intima may be stripped off, leaving the diseased tissue beneath. It thus contrasts strongly with the superficial fatty patches which result from fatty degeneration of the endothelial and sub-endothelial connective-tissue cells (p. 62).

In the earliest stage of the process a greyish, semi-translucent, round-celled infiltration is found between the laminæ forming the deeper part of the intima. This may go on to the production of fibrous tissue, a dense fibroid plaque or more diffuse thickening resulting; more often formation of fibroid tissue and fatty degeneration are found together (Fig. 105); or fatty degeneration and calcification may occur; or the fatty degeneration may lead to complete softening. Then a soft, yellowish, pul-

taceous material, consisting of fatty débris and cholesterin crystals, is found beneath the intima. This has been termed an **atheromatous abscess.** If the lining membrane perishes or is torn, the softened matters are carried away by the blood-stream, leaving an **atheromatous ulcer.** The middle and external coats become more or less infiltrated with leucocytes and converted into fibrous tissue.

FIG. 105.



Atheroma of the Aorta.—Showing the cellular infiltration of the deeper layers of the inner coat, and the consequent internal bulging of the vessel. The new tissue has undergone more or less fatty degeneration. There is also some cellular infiltration of the middle coat. *i.* Internal, *m.* middle, *e.* external coat of vessel. × 50, reduced ½.

It is not uncommon to find the arch of the aorta so studded with small, thickly-set, raised plaques that it looks somewhat like alligator-hide. The plaques are

yellow, many of them perhaps calcified, and the calcareous plates may be quite bare or covered by endothelium or a little fibrin; atheromatous abscesses and ulcers may also be present. The orifices of the coronary arteries are often more or less diminished by yellow rings around them, and the blood supply to the heart proportionately lessened.

It is obvious that changes of this kind will greatly impair the elasticity of a vessel and render imperfect the circulation in the parts beyond. Moreover, the inelastic vessel wall tends slowly to yield under the constant pressure to which it is subject. General dilatation of the vessel results; perhaps even a **fusiform** or **cylindriform aneurism.** When an atheromatous ulcer forms, the vessel is specially weakened at this spot, and a **sacculated aneurism,** or even rupture, may occur if the external coats have not been greatly strengthened by the formation of inflammatory tissue in them. And if the tissues round the margin of the ulcer have not been matted together by new tissue, the blood may find its way in the substance of the middle coat between the internal and external, forming a **dissecting aneurism.**

INFLAMMATION OF VEINS.

Inflammatory processes in veins are more frequent than in arteries, but here they are in the very great majority of cases **secondary** to coagulation of the blood within the vein (**thrombosis**), the coagulum exercising an injurious influence upon the coats of the vessel. These inflammations resulting from thrombosis have already been described (p. 231). They are localised or spreading, according as the clot is simple or continued (p. 233).

Other **causes** of phlebitis are violent **injury,** and **extension** of inflammation from adjacent tissues. Paget describes a gouty phlebitis especially common in the internal saphenous, and often recurrent.

The structural changes closely resemble those in the

arteries. In phlebitis from injury or from extension, the external and middle coats become infiltrated with cells, the vitality of the intima ultimately becomes impaired or lost, and when this has occurred the blood within the vein coagulates. In phlebitis from thrombosis the endothelium must suffer earliest.

CHAPTER XXXV.

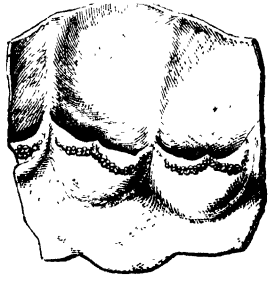
INFLAMMATION OF THE HEART.

INFLAMMATORY processes in the heart may affect the substance of the organ, or the endocardium. They are much more frequent in the last-named situation.

ENDOCARDITIS.

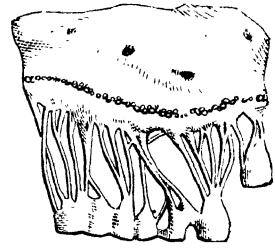
Endocarditis is for the most part limited to the valves of the heart, although it is occasionally met with in-

FIG. 106.



Inflammation of Aortic Valves. —The earlier stage of the process. Showing the situation of the inflammatory granulations.

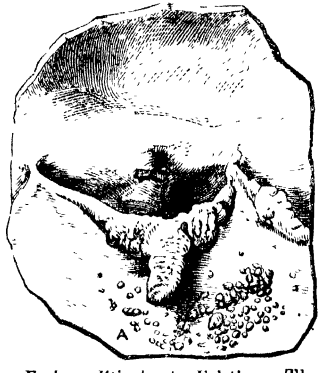
FIG. 107.



Inflammation of Mitral Valve. —The earlier stage of process. Valve seen from the auricular surface. Showing the situation of the inflammatory granulations.

volving more or less of the cardiac cavities. After birth the process is almost exclusively confined to the **left** side of the organ, and in the great majority of cases it commences in, and comparatively rarely extends beyond, the confines of the aortic and mitral valves and corresponding orifices. But during fœtal life, endocarditis is as exclusively confined to the **right** side (arterial), giving rise to congenital valve-lesions. It is those portions of the valves which come into contact in the act of closure, and are thus *most exposed to friction*, which are especially involved, and in which the changes usually commence. Thus, in the aortic valves, it is the convex surfaces of the segments which are most liable to be affected, and not the free edge of the segment, but the little band of tissue which passes from its attached border to the corpus Arantii in the centre (Fig. 106); and in the mitral valve, the auricular surface of the segments at a little distance from the attachment of the chordæ tendineæ (Fig. 107). When portions of the endocardium apart from the valves are affected, this is frequently due, as pointed out by Dr. Moxon, to the irritation caused by the friction of vegetations or fibrinous clots situated on the valves themselves (Fig. 108).

FIG. 108.



Endocarditis due to Friction.—The drawing represents a long vegetation on one of the segments of the aortic valve, which by rubbing on the endocardium below has produced numerous inflammatory granulations (A).

The histological changes accompanying endocarditis resemble those already described as occurring in those more chronic forms of arterial inflammation known as

atheromatous. The endocardium and inner coat of an artery are very analogous in their structure, both being non-vascular, and consisting of a layer of connective tissue with an internal endothelial covering. The inflammatory process may be acute or chronic.

ACUTE ENDOCARDITIS.—If the process be acute, the deeper layers of the endocardium become rapidly infiltrated with young cells, and as these increase in number the intercellular substance becomes softened and destroyed, and thus is produced a soft tissue composed almost entirely of cells such as always results from inflammatory processes in connective tissue. The new tissue as it increases projects through the superjacent endothelium in the form of minute granulations and vegetations upon the surface of the softened valve. (See Figs. 106 and 107.) The endothelial elements are said by some to participate in the active process. This is the **papillary** form of the disease.

FIG. 109.

Acute Endocarditis.—A granulation from the mitral valve, showing a fibrinous coagulum upon the surface of the granulation. × 10. (Rindfleisch.)

The above changes take place in an almost non-vascular tissue, and although there is more or less increase of vascularity in the external endocardial layers, where the capillaries are more numerous, there is rarely any redness or injection of the endocardium seen after death. The granulations, rough and bereft of endothelium, frequently induce coagulation upon themselves, and become covered by fibrinous caps. These must not be confounded with the vegetations themselves. (Fig. 109.)

The results of this cellular infiltration vary. If the process be very intense the new tissue may break down, and thus a loss of substance result—an endocardial ulcer. This takes place without any accumulation of cells sufficient to form an abscess, the new tissue simply becoming rapidly softened and disintegrating. In rare

cases, however, small quantities of pus are found in the deeper endocardial layers. The ulcer is irregularly defined, and its edges are usually swelled and thickened. This **ulcerative endocarditis** is, however, not frequent, the process usually being less acute. The ulceration may lead to perforation of the valve, or to a considerable destruction of its substance. Laceration or aneurism of the valve may also ensue from the pressure exercised by the blood against the damaged tissue. Sometimes the ulcerative process extends so as to involve the cardiac substance. Ulcerative endocarditis is a grave affection, often giving rise to embolism, and sometimes to a pyæmic process.

When the inflammatory process is less intense, as is much more commonly the case, the granulating valves may adhere to each other, or to an inflamed patch on the wall of the heart. The new tissue becomes incompletely organised into a fibrillated structure, whilst it undergoes, in part, fatty and calcareous degeneration. These changes always produce permanent **thickening, rigidity,** and **shrinking** of the valves, and consequent insufficiency, stenosis, or both. The new tissue may continue to grow after the severity of the process has subsided, and thus are produced the vegetations and papillary excrescences on the valve which are so commonly met with. (See Fig. 108.) These consist of a lowly organised tissue, which tends to undergo fatty and calcareous changes.

Etiology.—Endocarditis occurs especially in acute rheumatism; also in pyæmia, puerperal fever, gonorrœhal rheumatism, scarlatina, typhoid, and chronic Bright's disease. The papillary form is by far the commoner. The ulcerative may occur primarily, but as a rule supervenes upon the papillary or chronic forms.

The relation of endocarditis to the above diseases, and the course of the ulcerative form, suggests an infective origin. In ulcerative endocarditis many observers have found micrococcus-colonies on the vegetations and in

the substance of the valves. Köster and Klebs found them also in the papillary form. In some cases bacilli also have been found. In five cases of primary ulcerative endocarditis examined by B.-Hirschfeld, cocci only were present in all; and these organisms are demonstrable also in the secondary inflammations. In some cases no fungi have been found. No positive conclusion can be arrived at with regard to the etiology of the disease without culture- and inoculation-experiments.

CHRONIC ENDOCARDITIS.—This may be the sequel of acute inflammation, or the process may, from its commencement, be chronic in its nature. Conditions of mechanical strain, such as lead to chronic endarteritis, are the most important causes of chronic inflammation of the endocardium. The cell-infiltration is much less rapid and abundant than in the acute form; the intercellular substance consequently becomes much less softened and destroyed, and the new tissue has a much greater tendency to develop into a fibrillated structure. The result of these chronic processes is the production of a **fibroid thickening** of the endocardium, with considerable induration and contraction of the valves or valvular orifices. The new tissue sometimes forms papillary growths on the valves, which undergo partial fatty and calcareous changes. (See Fig. 108.)

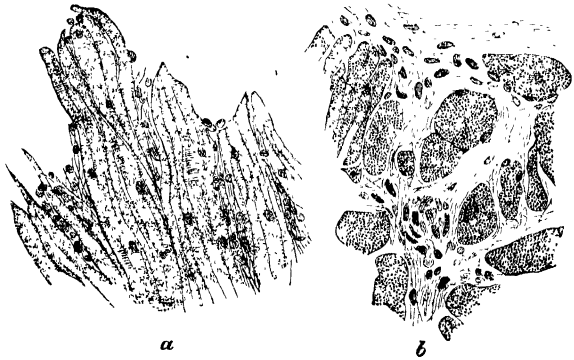
MYOCARDITIS.

Myocarditis, or inflammation of the cardiac substance, is much less frequent than the preceding. Intense and concentrated inflammations leading to the formation of abscess probably occur only as the result of a pyæmic process. Less intense and more diffuse forms of cardiac inflammation are also not unfrequently met with in association with pericarditis, and, less commonly, with endocarditis. Here the inflammatory process appears, by extension, to involve the immediately adjacent muscular layers of the organ, which are found infiltrated

with small cells, the fibres themselves being softened and granular.

In addition to the above, a form of myocarditis must be recognised in which the substance of the heart becomes more generally involved. In certain cases of acute rheumatism the muscular tissue of the heart is found after death swollen, softened, opaque, and occasionally faintly mottled with slightly yellowish patches. When examined microscopically, the fibres are seen to have lost their striation and to be finely granular, their nuclei are large and prominent, and small cells are found in varying

FIG. 110.



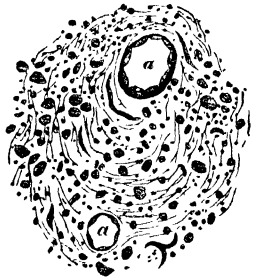
Acute Myocarditis.—From a case of acute rheumatism. *a.* A thin section of the left ventricle made in the direction of the muscular fibres, showing the granular and swollen condition of the fibres, and the prominence of their nuclei. *b.* A transverse section, showing the cellular infiltration of the intermuscular tissue. × 200.

numbers, infiltrating the intermuscular tissue. (Fig. 110). I have met with these appearances in two or three cases of acute rheumatism, and they must, I think, be regarded as evidence of the existence of an acute inflammatory process. The change is most marked in the left ventricle, and it is usually associated with endo- or peri-carditis. It is a grave complication of acute rheumatism, and

perhaps of some other diseases; it is probably more frequent than is generally supposed.

FIBROID INDURATION OF THE HEART.—This, a comparatively rare condition, is probably, in most cases, a result of chronic myocarditis. The change is characterised by the development of a fibrillated tissue between the muscular elements. The process commences in the intermuscular septa around the blood-vessels. This becomes infiltrated with small cells, which tend to develop into connective tissue. (Fig. 111.) The growth of new tissue gradually extends between the bundles of muscular fibres, so that ultimately each fibre may be surrounded by a tract of dense fibroid tissue. (Fig. 112.) The muscular fibres themselves, owing to the resulting interference with their nutritive supply, atrophy, undergo fatty metamorphosis, and are gradually replaced by the fibroid growth. (Fig. 112.) Very frequently the cellular nature of the growth, which I believe to characterise the earlier stages of its development, is not seen, the new tissue being simply fibroid.*

FIG. 111.



Fibroid Induration of the Heart.—A thin section from the wall of the left ventricle, showing the small-celled growth in the intermuscular septa around the blood-vessels. *a. a.* vessels. × 200.

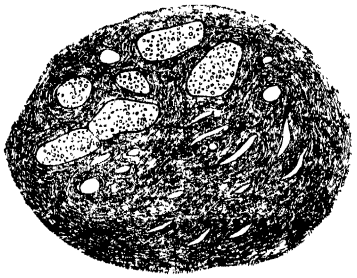
Fibroid induration of the heart appears in many cases to be induced by inflammatory processes commencing in the peri- or endo-cardium. When secondary to pericarditis, the change is usually most advanced in the more external portions of the cardiac walls, and it commonly affects both the right and left ventricles. When, on the other

* Dr. Hilton Fagge, in a series of eleven cases of fibroid disease of the heart, found that cellular elements in the new growth were almost invariably absent. (See *Trans. Path. Soc. Lond.*, vol. xxv. p. 64.)

hand, an endocarditis is the precursor of the indurative process, the change is more marked in the internal muscular layers, and inasmuch as inflammatory processes in the endocardium occur almost exclusively in the left cardiac cavities, the left ventricle is principally involved. In other cases the fibroid growth appears to be the result of syphilis. (See "Syphilis.")

Although the growth of new tissue is thus usually more advanced in certain portions of the muscular walls than in others, it is by no means uniformly distributed. In some parts it may be very dense, the muscular fibres

FIG. 112.



Fibroid Induration of the Heart —A section from the left ventricle of the same heart as Fig. 111, showing a more advanced stage. The fibroid tissue surrounds the individual muscular fibres, which are undergoing fatty degeneration. × 200.

being entirely obliterated, whilst in others it is entirely wanting, and the muscular elements present a normal appearance.

The cardiac walls may become much thickened by the new growth, and the induration of texture is often very considerable. In the specimen from which the accompanying drawings were made the walls of the left ventricle were so hard that they cut almost like a piece of tendon.

Fibroid induration of the heart—excluding that resulting from syphilis—appears to occupy the same patholo-

gical position as similar fibroid changes in other organs *e.g.*, in the liver and kidneys. It must therefore be regarded as the result of a chronic inflammatory process —a chronic myocarditis. Its effect must evidently be to interfere very materially with the motor power of the organ, and it consequently constitutes one of the most grave of all the cardiac diseases.

CHAPTER XXXVI.

INFLAMMATION OF LYMPHATIC STRUCTURES.

Inflammatory processes in lymphatic structures usually result from their injury by substances conveyed to them by the lymphatic vessels. They include—**acute** and **chronic** inflammations, and the specific inflammations associated with **Typhoid Fever.** Each of these must be considered separately.

ACUTE INFLAMMATION OF LYMPHATIC STRUCTURES.

Examples of acute inflammation of lymphatic structures are furnished by the inflammation of the glands in the axilla from a wound on the hand, of the glands in the groin from gonorrhœa, and of Peyer's and the solitary glands in the intestine from inflammation of the intestinal mucous membrane.

Inflammation of lymphatic glands is almost always due to absorption of some infective substance from a primary focus of inflammation (diphtheritic, erysipelatous, scarlatinal, chancrous, &c.); micro-organisms have frequently been demonstrated in them. A gland affected by acute inflammation becomes intensely vascular and the seat of

free exudation. The escaping leucocytes accumulate in its tissues and sinuses, until all distinction between medulla and cortex has disappeared, and the gland substance is soft and pulpy, and perhaps strewn with hæmorrhages. Leucocytes in the lymph coming from the primary focus are also detained in the gland.

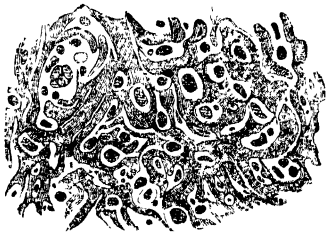
Upon the removal of the injurious influence the process may gradually subside, the new elements undergo disintegration and absorption, and the gland returns to its normal condition (Resolution).

In other cases the process goes on to suppuration, the trabeculæ are destroyed, many of the cells become disintegrated, and the loculi of the gland become filled with pus. This is usually associated with inflammation and suppuration of the surrounding connective tissue. In the glands of a mucous membrane the process gives rise to what is known as a follicular abscess. In still more acute cases the inflammation may be truly hæmorrhagic.

CHRONIC INFLAMMATION OF LYMPHATIC STRUCTURES.

Chronic inflammations of lymphatic structures result from injuries which are less severe and more prolonged in

FIG. 113.



Chronic Inflammation of a Lymphatic Gland.—Showing the increase in the stroma, and the diminution in the number of the lymphoid cells. × 200.

their action than those which give rise to the acute form. The resulting cellular infiltration of the gland is conse-

quently a more continuous one, and the gland becomes more or less permanently increased in size. The reticulum is also considerably involved. These chronic inflammatory processes differ from the acute, inasmuch as they lead to a gradually increasing development of the reticular structure of the gland. The reticulated network becomes thicker and more fibrous, its meshes become smaller and smaller, the lymph-cells diminish in number, and thus the gland becomes hard and fibrous in consistence. (Fig. 113.) Perhaps, in these chronic cases, the cells of the gland-substance, and the flat connective-tissue cells covering the trabeculæ multiply and assist in forming the infiltrating cells; but it is difficult to prove. Fatty patches are frequent in chronically inflamed glands.

Scrofulous Glands.—In those chronic inflammations of the lymphatic glands which occur in scrofulous subjects, and in which the glands tend to become caseous, the changes resemble those which have been already described as characteristic of scrofulous inflammation. (p. 340.) The cell-infiltration is considerable, there is but little tendency to absorption, and many of the cells increase in size, and even form multi-nucleated elements. The gland thus becomes enlarged, soft, and elastic in consistence, and of a uniform greyish-white colour. Owing to the obstruction to the circulation caused by the pressure of the cellular infiltration, the gland undergoes retrogressive changes and becomes caseous. The caseous material may subsequently liquefy, or become infiltrated with calcareous particles. Many caseous lymphatic glands are tuberculous (p. 313), and the Bacillus tuberculosis is found in them in small numbers.

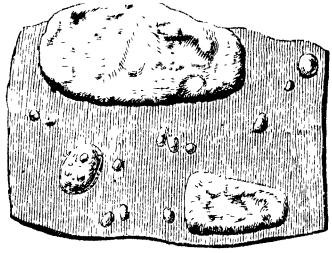
INFLAMMATION OF LYMPHATIC STRUCTURES IN TYPHOID FEVER.

The inflammatory processes which occur in the lymphatic structures in typhoid fever have their seat in the spleen, in the lymphatic structures of the intestine, and in the mesenteric glands.

The Spleen.—In the spleen the change resembles that which occurs in many of the other acute febrile diseases, although it reaches its maximum in typhoid. The splenic tissue becomes exceedingly vascular, and the lymphatic elements increase rapidly in number, so that the organ often attains two or three times its natural size. Many of the new elements enter the blood, thus causing a slight temporary increase in the number of white blood-corpuscles. As the fever subsides, the hyperæmia diminishes, many of the new elements undergo disintegration and absorption, the remainder enter the blood, and thus the organ again attains its normal characters and dimensions.

The Intestinal Lymphatic Structures.—It is in the solitary and Peyer's glands that the most characteristic changes take place in typhoid fever. These structures may be involved throughout the whole of the small and large intestine, but in most cases the process is limited to those in the ileum and cæcum; and those glands are always the most affected which are situated the nearest to the ileo-cæcal valve.

FIG. 114.



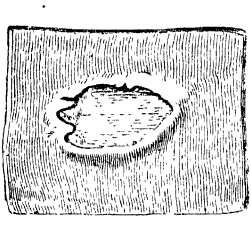
Typhoid Swelling of Peyer's Patches and Solitary Glands of the Intestine.

The primary change here consists in a hyperæmia and cellular infiltration of the glands. Many of the cells increase considerably in size, so as to form the multi-

nucleated elements already alluded to. Both Peyer's patches and the solitary glands thus become considerably enlarged and prominent, standing up above the surface of the intestine. (Fig. 114.) They are of a greyish-white or pale reddish colour, and of a soft, brain-like consistence. The surrounding mucous membrane is also exceedingly vascular, and is the seat of an acute catarrhal process. This catarrh is more or less general, and usually precedes the swelling of the glands. The cellular infiltration, in many parts, rapidly extends beyond the confines of the glands into the immediately surrounding and subjacent tissues, and in some cases even into the muscular coat.

The process now passes into the second stage—that of the death and disintegration of the newly formed tissue. This may terminate in various ways. Many of the enlarged glands subside, the new elements become disintegrated and are absorbed, and the inflammation thus undergoes a gradual process of **resolution.** In others, the individual follicles of the gland rupture, discharging their contents externally, and the patches then acquire a peculiar reticulated appearance. The most characteristic termination, however, of the typhoid process is the separation of the dead tissue as a slough, and the formation of the **typhoid ulcer.**

FIG. 115.



A Typhoid Ulcer of the Intestine.

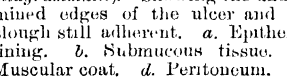
The process of sloughing and ulceration may, like the cellular infiltration, take place uniformly throughout the whole gland, in which case the whole mass is thrown off, leaving an ulcerated surface corresponding in size with that of the gland. (Fig. 115.) More commonly, however, the sloughing commences in different portions of the patch, and small irregular losses of substance result,

which may gradually extend until they form one large ulcer.

Although, as already stated, the cellular infiltration may extend beyond the confines of the glands, this is rarely the case with the ulceration. The peripheral infiltration undergoes resolution, and hence the ulcers have the same configuration as the original glands; those originating from the patches being oval, with their long diameter in the direction of the gut; and those originating in the solitary glands being spherical in shape. In rare cases, when there is much infiltration of the surrounding mucous membrane, the ulceration may extend slightly beyond the confines of the glands.

With the sloughing and disintegration of the new tissue the process of infiltration ceases, and hence there is no induration or thickening of the base or edges of the ulcer. The base is smooth, and is usually formed of the submucous or muscular coat of the intestine. The edges are thin and undermined, and consist of a well-defined fringe of congested mucous membrane. (Fig. 116.) This is best seen when the gut is floated in water. In some cases, however, the sloughing extends deeper through the muscular layer to the sub-peritoneal tissue, and it may thus cause perforation and peritonitis.

FIG. 116.



A Typhoid Ulcer of the Intestine (diagrammatic).—Showing the undermined edges of the ulcer and the slough still adherent. *a.* Epithelial lining. *b.* Submucous tissue. *c.* Muscular coat. *d.* Peritoneum.

The third stage of the process is that of cicatrisation. This takes place by the resolution of the peripheral infiltration, the approximation and union of the undermined edges with the floor of the ulcer, and the gradual formation from the margin of an epithelial covering. The gland-structure is not regenerated. The resulting cicatrix is slightly depressed, and less vascular than the surrounding mucous membrane. There is no puckering

or diminution in the calibre of the gut. In some cases, however, cicatrisation does not take place so readily, and the floor of the ulcer becomes the seat of a **secondary** ulceration. This usually takes place after the general disease has run its course, or during a relapse. Profuse hæmorrhage and perforation more commonly result from the secondary ulceration than from the primary sloughing of the glands.

The Mesenteric Glands.—The change in the mesenteric glands is probably secondary to that in the intestine. These glands become the seat of an acute cellular infiltration, and are enlarged, soft, and vascular. They usually, like many of the glands in the intestine and the spleen, undergo a gradual process of resolution. In rare cases, however, the capsule of the gland is destroyed, and the softened matters may escape into the peritoneal cavity and so cause peritonitis. The enlarged glands may also become caseous, and subsequently calcified.

Bacilli of characteristic form have been found in the ulcers and mesenteric glands, and also in blood taken from the spleen during life.

CHAPTER XXXVII.

INFLAMMATION OF MUCOUS MEMBRANES.

Inflammations of mucous membranes are divided into **catarrhal, croupous**, and **diphtheritic.**

CATARRHAL INFLAMMATION.—This may, according to its intensity, be serous, mucous, muco-purulent, or purulent. Acute cases begin with redness, slight swelling, and abnormal dryness of the mucous membrane, some tenderness of the part, and perhaps pain. After a time this is succeeded by exudation, and the symptoms are then as a rule relieved. In chronic cases, the symp-

toms and physical signs are much less marked, the exudation being generally the first thing noted. Post-mortem, all hyperæmia has generally disappeared, and the membrane may look paler than natural; but after chronic inflammation of any intensity, more or less dark-grey pigmentation, from the hæmoglobin of extravasated red corpuscles, will, in most situations, bear evidence of former inflammation (p. 102). These appearances can be studied nowhere better than in the inflamed bladders from cases of stricture, enlarged prostate, &c.

Serous Catarrh.—Free serous effusion occurs from the vessels and escapes upon the surface; this is often seen in the early stage of colds in the head.

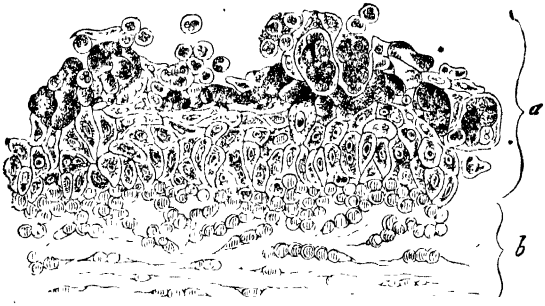
Mucous Catarrh is characterised mainly by increased production of mucus, which escapes mixed up with serous fluid, or remains adherent to the surface, as is often seen in chronic pharyngitis. Sometimes the sero-mucous discharge is tolerably clear, at others more or less opaque; in the former case, only a moderate number of cell-forms are present—in the latter, many. Most of the cells are escaped leucocytes, but many are desquamated epithelial elements. The increased "secretion" of mucus and the excessive desquamation of epithelium have been looked upon as disproving the view that depression of function is an invariable result of inflammation. The formation of mucus, however, is much more a degeneration than a secretion, and such a process might well be hastened by irritation. With regard to the epithelial cells—it would seem likely that, whilst the superficial layers are killed by the irritation and cast off, the deeper ones are more resistant even than the elements of the superficial vessels. The action of an irritant which causes the latter to leak gravely, leaves the former able to multiply freely. Indeed, it is conceivable that what would be an irritant to one cell might be a stimulant to another more resistant organism, rendering it more capable of utilising increased supply of food.

Purulent Catarrh.—If the inflammation be more

intense, the escape of leucocytes is still greater, and the secretion becomes purulent. As the exudation approaches more and more closely the character of true pus, the formation of mucus and the desquamation of epithelium cease — a **muco-purulent** stage being often passed through.

A section through a mucous membrane thus affected (Fig. 117) shows desquamation of the superficial epithelial

FIG. 117.



Catarrhal Inflammation of the Conjunctiva. —*a*. Epithelium. *b*. Infiltrated sub-epithelial connective tissue.—Showing the desquamation of the epithelium, and the young elements within the epithelial cells. (Rindfleisch.)

cells, and these often contain broods of young cell-leucocytes which have migrated into them. Leucocytes lie here and there between the deeper cells, in which evidence of multiplication will be found. More or fewer white corpuscles infiltrate the mucosa, together with fluid exudation, producing swelling of it; or thickening and induration, if they go on to form connective tissue.

Simultaneously, all lymphoid structures in the mucous membrane are affected. The lymph-follicles swell, and their contents may soften and form minute abscesses, which burst and leave the small ulcers (follicular), so often seen in catarrhal conditions of the intestines and pharynx. The ulceration in some cases extends beyond the confines

of the follicle. The proper glandular structures also may become involved. Their epithelium multiplies, the glands become choked with the epithelial elements, and they may subsequently atrophy. This is seen in catarrh of the stomach.

The acute process may quickly subside, or it may become chronic. In the latter case the hyperæmia diminishes, but the escape of leucocytes and the multiplication of the epithelial elements continue, and the sub-epithelial tissue becomes more extensively infiltrated with small cells.

Chronic catarrhal inflammations of mucous membranes differ from the acute, inasmuch as the sub-epithelial connective tissue is often extensively infiltrated with small cells, which may ultimately form an imperfectly fibrillated structure. The membrane thus becomes indurated and thickened, and the pressure exercised by the new growth may induce atrophic changes in the glandular structures which it contains, as is seen in chronic catarrh of the stomach; by preventing the exit of their secretion it may cause them also to dilate so as to form cysts. These changes in the sub-epithelial connective tissue are usually accompanied by enlargement of the lymphatic structures, an enlargement which sometimes gives to the membrane a nodular or granular appearance. This is well seen in the pharynx (follicular pharyngitis). The enlarged lymphatic structures may ulcerate and constitute the starting-point of an infective process. (See "Tuberculosis of Mucous Membranes.") In some situations, as the stomach and intestine, the membrane often at the same time becomes deeply pigmented.

CROUPOUS AND DIPHTHERITIC INFLAMMATION.—These terms are applied to inflammations of mucous membranes and raw surfaces which lead to the production of a so-called **false membrane**—such as is seen, for example, in croup. The formation of this fibrinous layer upon the surface of the membrane is quite characteristic, and at once distinguishes this form of

inflammation from a simple catarrhal process. On mucous surfaces, the membrane may exist in little patches or cover a large area; it is usually of a yellowish or greyish-white colour, and in consistence varies from a firm and tough to a soft pultaceous material. It may be deeply blood-stained. It is with greater or less difficulty separable from the subjacent tissue, which in all cases after its removal is found to have lost its epithelium. In thickness it may vary considerably in different parts.

The two words—croupous and diphtheritic—owe their origin to the belief, still held by many, that there is an idiopathic membranous inflammation of the larynx (croup) distinct from diphtheria. Croup had long been known when Bretonneau, in 1826, first accurately described diphtheria, gave the disease its present name, and asserted that "croup" was merely laryngeal diphtheria. The term is used with this meaning in France, and the majority of English physicians adopt Bretonneau's view. The adjectives, croupous and diphtheritic, are often used as synonymous, but many propose to speak of a membrane as **croupous,** when it involves no more than the epithelium of a mucous membrane, as **diphtheritic,** when it involves the mucosa. These differences in the depth of the tissue involved are probably due to variations in the intensity of the process; and, according to Cohnheim, the process is more likely to be superficial in those situations where a distinct basement membrane exists—as in the pharynx and respiratory tract—than in those where this is not the case, as in the intestines and conjunctiva. A false membrane superficial to the basement membrane is much more easily detached than one which involves this structure.

Others would limit the term "croupous" to false membranes formed chiefly of coagulated fibrin, whilst "diphtheritic" is applied to those consisting of tissues which have undergone coagulation-necrosis (p. 288). This division, which renders "croupous" equivalent to "fibrinous," seems to be the better, although the two processes

—coagulation of fibrin and of cells—are closely allied, and one may succeed the other in the same case.

The relative rarity of fibrinous inflammations of mucous, as compared with serous, membranes led Weigert to investigate the reason of the difference. He found that inflammatory exudations from mucous membranes coagulated so soon as the epithelium was destroyed, and he started the hypothesis that *living* epithelium, like endothelium, prevents the formation of fibrin.

But the injury which causes destruction of epithelium must be more intense than one which does not cause such damage; and it is likely that the exudation in the former cases will be more highly fibrinous than in the latter. Now, in a case of true diphtheria, a patch of epithelium and more or less of the subjacent tissue are killed by the irritant and undergo coagulation-necrosis; and, if the false membrane thus formed be removed, a fresh one will form rapidly, which, unless the destruction of tissue extends, can hardly consist of anything but coagulated fibrin.

The two kinds of membrane differ microscopically. The fibrinous has the appearance of lymph—a network of fibrin containing in its meshes a greater or less number of leucocytes, desquamated epithelial cells, and débris; it is easily stripped off. The diphtheritic membrane is separated less easily, and, if deep, only with great difficulty. Superficially it closely resembles the croupous membrane, but the deeper parts consist of much swollen, homogeneous cells, from which the nuclei have disappeared. There is no sharp line in advancing cases between the coagulated and the living tissue-elements. These membranes resist acetic acid much longer than do the simple fibrinous ones.

False membranes probably form occasionally upon every mucous membrane, and obviously from very different causes. Examples are:—the membranes which form on the tonsils, larynx, &c., in true diphtheria; from scalds and the application of caustic chemicals; in the bladder after

parturition (when a complete cast may be expelled), and in the most acute cystitis; in the vermiform appendix, sometimes from the irritation of a concretion; in the lower part of the large intestine in dysentery; and in the air-tubes in plastic bronchitis. It may be noted here that false membranes sometimes form upon granulating wounds (croup of granulations), and it is held by some that there is no line between such cases and those of true diphtheria of wounds and of hospital gangrene. It seems most probable, however, that there is an etiological difference, for croup of granulations may be induced at will by blistering the surface.

Although the above facts show that false membranes may result from the action of simple irritants, the great majority met with in Man are due to **infective** poisons—*e.g.*, diphtheria, diphtheritic conjunctivitis, epidemic dysentery—all highly contagious. Micrococci, with other organisms, are found in clouds and zoogloea masses in almost all cases; but no etiological connection has been established between them and any of these diseases.

DYSENTERY.

The inflammatory processes occurring in the intestine in dysentery are for the most part limited to the large intestine, although the ileum is also occasionally involved. The inflammation is always most marked in the rectum and descending colon, and it may be stated generally that it is characterised by the ulceration and sloughing of the membrane to which it gives rise.

The intestinal changes vary considerably, according to the intensity of the inflammatory process. In the milder forms of the disease, the changes are most marked on the summits of the folds of the mucous membrane. These are found covered with a greyish-white layer of fibrinous-looking material, which, when scraped off, leaves a superficial loss of substance. The mucous membrane generally is hyperæmic and softened. The submucous tissue also

is infiltrated with inflammatory products, and the solitary glands are enlarged and prominent.

When the process is more severe, the submucous tissue becomes more extensively involved, and the superficial layer of fibrinous material extends over wider areas and implicates more deeply the mucous membrane. The thickening of the intestinal wall, however, is much greater in some parts than in others, so that projections are produced upon the inner surface of the intestine, corresponding with those parts which are the most affected. The enlarged solitary glands usually slough, and so give rise to circular ulcers, which rapidly increase. When the process has reached this stage, the muscular and serous coats are implicated, the latter being covered with layers of fibrin which form adhesions with adjacent parts. The intestine is much dilated, and contains blood and disintegrating inflammatory products.

In the most intense forms of the disease the necrosis is more extensive. According to Rokitansky, large portions of the mucous membrane are converted into black rotten sloughs. The submucous tissue is infiltrated with dark blood and serum, but subsequently it becomes the seat of a reactive suppurative inflammation, by means of which the necrosed portions of tissue are removed.

If death does not occur, and the inflammatory process subsides, the ulcers may gradually heal. When the loss of substance has not been considerable, the edges of the ulcers may, by the contraction of the submucous tissue, become completely approximated. More commonly, however, the loss of substance is so great, that portions of the membrane are left, consisting simply of connective tissue.

When the inflammatory process becomes chronic, the changes in the submucous connective tissue become more marked, and the new fibroid growth gives rise to considerable thickening and induration of the intestinal wall, and to more or less contraction and narrowing of the cavity. Sometimes it forms fibrous bands, which project

into the gut. The formation of abscesses and fistulous passages occasionally occurs in the thickened intestinal wall.

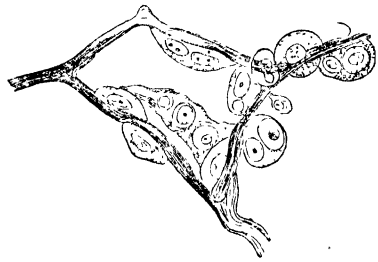
CHAPTER XXXVIII.

INFLAMMATION OF SEROUS MEMBRANES.

Inflammatory processes in serous membranes vary in their intensity, and in the amount and character of the effusion.

The process commences, as in mucous membranes, with hyperæmia, and exudation of fluid and of blood-

Fig. 118.



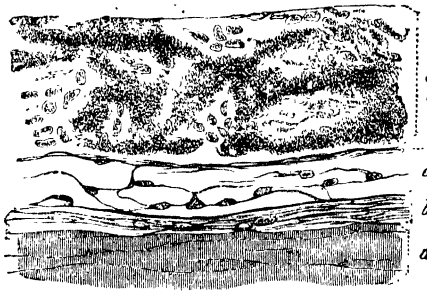
Inflamed Epiploon of a Rabbit.—Showing changes in the endothelium. × 250. (Cornil and Ranvier.)

corpuscles into the serous cavity quickly follow. (Fig. 118.)

Next to hyperæmia, the first sign of inflammation is a loss of polish of the surface, owing partly to the injury done to the epithelium by the irritant, and to the passage out through the layer of cells of the exudation, partly to the presence of leucocytes and a little fibrin on the surface. The moistening of the surface with the albuminous

exudation renders it "greasy." As the inflammation goes on, the surface becomes opaque, roughened, and exceedingly vascular; and soon it becomes covered with a fibrinous layer, whilst more or less liquid transudes into its cavity. The coagulable material which exudes from the vessels forms a soft, elastic, membranous, or reticulated investment, inclosing in its meshes numerous small cells. This either glues the two surfaces of membrane together, collecting especially where pressure is least, viz., along the angles of contact of the intestines, where injection also is most marked; or, if they are separated by liquid effusion, forms a slightly adherent layer. (Fig. 119.) The exuded liquid varies considerably in amount, and is

FIG. 119.



Inflammation of the Diaphragmatic Pleura.—Showing the adherent fibrinous layer. *a.* Muscular coat of diaphragm. *b.* Sub-serous tissue. *c.* Serous membrane. *e.* Fibrinous layer. × 400. (Rindfleisch.)

always turbid, thus differing from non-inflammatory effusions. It contains flakes and masses of coagulated fibrin and innumerable cells, the latter being in the earliest stages of the process almost entirely emigrants.

The nature of the subsequent changes will depend upon the intensity of the inflammation, and upon the amount of liquid exuded into the serous cavity. If the inflammatory process subsides, and the liquid exuded is

not sufficient to prevent the two surfaces of the membrane from coming into contact, they grow together and form an adhesion. This constitutes the so-called **adhesive inflammation.** The union is effected by the formation of connective tissue (p. 275). This is by far the most frequent form of inflammation of serous membranes. The process is precisely similar to that which takes place in the union of an incised wound. It is probable also that in some cases union may take place without the intervention of any fibrinous layer, by the formation and growing together of irregular papillary outgrowths from the sub-endothelial tissue.

If, however, the inflammatory process is severe, or the surfaces of the membrane are separated by a large quantity of liquid effusion, organisation and adhesion cannot be effected. If a large quantity of liquid exists in the serous cavity, the removal of this becomes necessary before union can take place. If the intensity of the irritant is considerable, and its action prolonged, union is prevented by the formation of pus. These two conditions must be considered separately.

The existence of a large amount of effusion prevents approximation, and therefore adhesion, of the serous surfaces, and before this can be effected absorption of the liquid becomes necessary. The presence of the liquid itself, however, interferes with its absorption. This is owing, as already stated (pp. 286–7), to the pressure which it exercises upon the blood-vessels and lymphatics; which pressure, by hindering the circulation in these vessels, tends not only to prevent absorption, but also to interfere with the restoration of the vascular walls to a normal state, and so to favour a continuance of the exudation. The removal of some of the liquid by artificial means consequently facilitates absorption of the remainder. When the process is protracted, the sub-endothelial connective tissue becomes involved and infiltrated with small cells, and a richly vascular granulation-tissue is formed beneath the layer of proliferating endothelium. The endothelium

itself becomes less abundant, and, if the inflammation subsides, the new granulation tissue gradually develops into connective tissue, and thus a false membrane is formed, rich in vessels, which takes the place of the endothelial layer. As the liquid is absorbed, the two surfaces of the membrane come into contact and grow together, the new vessels becoming gradually obliterated.

If the inflammatory process does not subside, or is from its commencement of considerable intensity, it may be attended by the formation of large quantities of pus. In this case the exudation of blood-corpuscles is so considerable that the young elements exist in large enough numbers to give to the exuded liquids a purulent character. The condition is then termed **empyæma.** As the connective tissue becomes involved, a granulation tissue is formed; and this may continue to generate pus like an ordinary granulating wound. If the pus be removed, the suppuration may gradually cease, the granulation tissue develop into a fibrous structure, and the union of the serous surfaces thus be effected. The serous membrane becomes greatly thickened, and the new tissue undergoes considerable contraction in the process of its organisation, producing more or less retraction of the chest-wall.

CHAPTER XXXIX.

INFLAMMATION OF THE LIVER.

INFLAMMATORY processes in the liver comprise—**perihepatitis, abscess,** and **cirrhosis.**

PERIHEPATITIS.

Inflammation of the capsule of the liver leading to more or less thickening, and often to adhesions with

adjacent parts, is met with under various circumstances. Its most common causes are—the chronic peritonitis of Bright's disease, chronic alcoholism, and syphilis (Goodhart). The changes are usually slight and of but little pathological import.

In some cases, however, especially in cases of chronic peritonitis (Hilton Fagge), the process is more extensive and leads to marked interference with the functions and circulation of the liver. The whole capsule becomes considerably thickened and gradually contracts, thus causing compression of the organ, which assumes a globular form. The portal circulation is often interfered with by the squeezing process, and ascites with other symptoms of portal obstruction may result. The liver itself with the exception of some atrophy and fatty degeneration of its cells may show no changes; but sometimes it is intersected by bands of fibrous tissue passing inwards from the capsule. The latter suggests syphilis as the cause (see p. 338).

HEPATIC ABSCESS.

Acute inflammation of the liver leads to the formation of abscess. The abscess may be **single** or **multiple**. The latter are usually small, but a solitary abscess may attain an enormous size. **Multiple** abscesses are most frequently due to pyæmia, or to some inflammatory lesion in connection with the portal system—such as dysentery. In these cases the abscess is of embolic origin. Inflammation of the bile-ducts, such as sometimes results from gall-stones, &c., and external violence, are other causes of suppurative hepatitis.

The **solitary** or **tropical** abscess also is supposed by some to be secondary to some inflammation of the portal viscera. It is known to be often associated with dysentery. It is maintained by many that it is due to a primary hepatitis, and doubtless cases often occur in which no intestinal ulcer or other obvious cause is discoverable.

The pathology of this disease is, however, at present obscure.

CIRRHOSIS OF THE LIVER.

Chronic inflammation of the liver constitutes the condition known as **Cirrhosis**. This is characterised by a gradual increase in the connective tissue of the organ, and by the subsequent atrophy of the liver-cells, so that when examined with a low magnifying power

FIG. 120.

Cirrhosis of the Liver.—Showing the growth of connective tissue between the hepatic lobules. *a*. Lobules. *b*. New growth of interlobular connective tissue. × 16.

the lobules are seen to be separated by new interstitial growth. (Fig. 120.)

HISTOLOGY.—The process, like that of chronic inflammation in other organs, consists essentially in a cellular infiltration of the interlobular connective tissue of the liver, and the development of a more or less highly organised fibroid structure; the number of cells being proportionate to the activity of the process. The new tissue is supplied with new blood-vessels, derived from branches of the hepatic artery.

In addition to this cellular infiltration of the interlobular connective tissue, a proliferation of the bile-ducts is supposed to occur frequently in cirrhosis. This is believed by Charcot to take place in those cases only in which there exists some obstruction of the ducts—the so-called "Biliary Cirrhosis." (See "Etiology.") Other observers, however, state that new ducts are met with under such various circumstances that their existence is of no etiological value. Goodhart doubts the formation of *new* ducts, but thinks the old ones simply become more conspicuous owing to the atrophy of the liver-cells.*

The liver-cells are stated by many to undergo active changes, and to contribute to the formation of the new tissue. They are in many cases infiltrated with fat— **fatty infiltration** being associated with the cirrhosis. (See Fig. 122.)

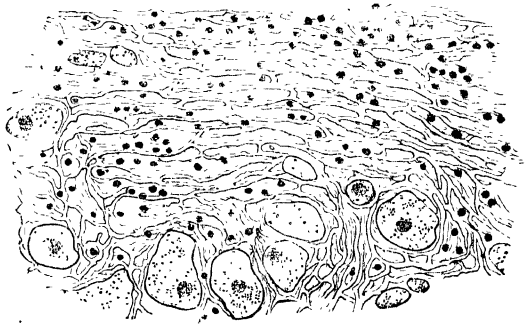
The general distribution of the new tissue is described by Charcot as—**multilobular, unilobular,** and **intercellular.** In the multilobular form, groups of lobules are surrounded; in the unilobular, each lobule; and in the intercellular, the growth invades the intercellular network. These several modes of distribution are frequently associated, all perhaps being found in different parts of the same organ; and although supposed by Charcot to indicate etiological varieties, the differences are probably to be ascribed rather to differences in the activity of the growth; the more active the process, the more uniform and general the distribution.

The effect of the new growth is ultimately to cause atrophy of the hepatic cells, and to obstruct the circulation through the portal capillaries and the passage of bile through the bile-ducts. This effect is materially increased by the process of contraction which the new tissue undergoes. The hepatic cells in the outer zone of the lobules are the first to atrophy. The cells become

* The subject is ably discussed by Dr. Goodhart in his "Résumé of Diseases of Liver," *New Sydenham Soc. Atlas of Path.* Fas. iv.

smaller, often undergo fatty metamorphosis, and ultimately are completely destroyed. (Fig. 121.) Those in the central parts of the lobule are in the earlier stages but little altered, although they are often stained with bile. As the growth extends, however, these also become annihilated, and the whole lobule may be replaced by connective tissue. The cells in the outer part of the

FIG. 121.



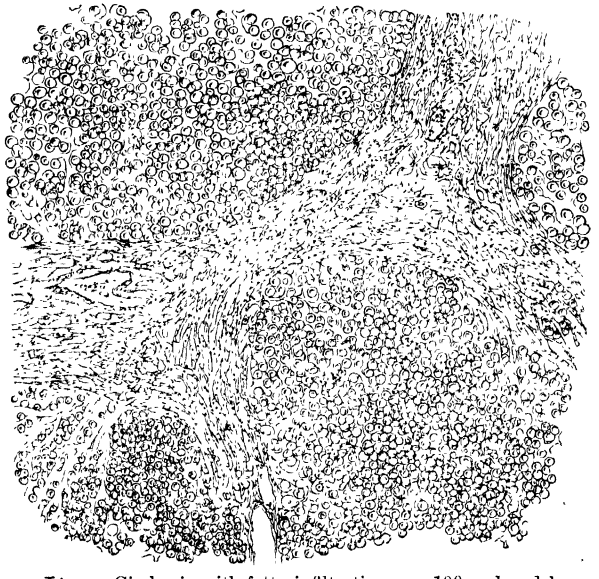
Cirrhosis of the Liver.—A thin section from the external portion of one of the hepatic lobules.—Showing the new growth of connective tissue, and the way in which it involves the intercellular network and causes atrophy of the liver-cells. × 200.

lobules are sometimes, as already stated, infiltrated with fat prior to their destruction. (See Fig. 122.)

Physical Characters.—The physical characters of the cirrhosed liver vary. In the earlier stages of the disease the organ is probably always more or less increased in size; the enlargement being almost uniform, and the edge rounded and thickened. This enlargement very often exists up to the end of the disease, but in many cases the atrophy of the liver-cells and the contraction of the new tissue lead to considerable diminution in size. The surface of the organ is usually more or less irregular, sometimes "hobnailed;" the extent of the irregularity

depending upon the distribution of the new tissue and the amount of atrophy that has taken place. A multilobular distribution leads to much greater unevenness of the surface than a unilobular one. The consistence of the organ is always more or less increased, although in some cases, where the process is very rapid, the increase is so slight as easily to escape observation. On section, the new tissue is often visible to the naked eye surrounding

FIG. 122.



Liver.—Cirrhosis with fatty infiltration. × 100, reduced ⅓.

the lobules, and in many parts completely replacing them. This gives to the cut-surface a mottled granular appearance, the lobules themselves contrasting with the new interlobular tissue; and this appearance is sometimes increased by fatty infiltration of the cells in the peri-

pheral zone. The capsule also may be thickened, and the organ is frequently stained with bile.

The great increase in the size of the liver which exists in some cases is due in part to a fatty infiltration of the liver-cells. (Fig. 122.) In those cases, also, in which the process is rapid, and the new growth consequently very general in its distribution—unilobular and often intercellular—the organ is usually large; death probably supervening before time has been allowed for much atrophy and contraction to take place. Some of the large livers are supposed to be due to obstruction of the bile-ducts, and have been termed "biliary" or "hypertrophic" cirrhosis. The existence of such a condition is disputed by some, especially by Goodhart.

ETIOLOGY.—The great cause of cirrhosis is alcohol. With the exception of syphilis no other cause can be regarded as proven. The question of a biliary cirrhosis must at present remain an open one. Cirrhosis from syphilis has already been described (p. 339). In the congenital disease the process is often so general in its distribution as closely to resemble some cases of acute alcoholic cirrhosis.

It is important to remember clinically that cirrhosis not only obstructs the portal circulation, thus giving rise to ascites, hæmatemesis, diarrhœa, enlargement of the spleen, &c.; but that, owing to the destruction of the liver-cells, the glycogenic function of the organ is so much impaired that marked interference with general nutrition results.

ACUTE YELLOW ATROPHY.

This exceedingly rare disease of the liver is characterised by a rapid diminution in the size of the organ, accompanied by destruction of the hepatic cells. The liver may, in the course of a few days, be reduced to less than half its natural bulk, being especially diminished in thickness. It is soft and flabby in consistence, bloodless, and of a

dull yellow or yellowish-red colour. The lobules are indistinguishable. When examined microscopically, the liver-cells are found to be completely destroyed, being replaced by granular débris, fat granules, and pigment. Tyrosin and leucin have been found in the disintegrated liver-tissue. The pathology of this disease is exceedingly obscure. By some it has been regarded as a passive degeneration, by others as an acute infective inflammation. Micrococci have been found in the organ in early stages of the disease by Dreschfeld and others.

CHAPTER XL.

INFLAMMATION OF THE KIDNEY.

Inflammatory processes in the kidney present certain variations according to their intensity: They comprise **suppurative, tubal,** and **interstitial** nephritis. Of these, suppurative nephritis, as the name implies, is an intense inflammation leading to the formation of abscess; and it is really an acute interstitial inflammation, although the term "interstitial" nephritis is generally applied to chronic processes. It results usually from the transmission of infective materials from some primary lesion (pyæmic), or is associated with some inflammatory condition of the lower urinary passages. Tubal nephritis is also an inflammation of considerable intensity, and in it the structural changes have their principal seat in the urine-tubes. Interstitial nephritis is an inflammatory process which runs a more chronic course, and is of less intensity than either of the preceding; consequently in it the principal structural changes take place in the connective tissue around the blood-vessels—in the intertubular connective tissue (p. 278). It must, however, be distinctly borne in mind that these two varieties of histological changes—those in the tubes and those in the intertubular

connective tissue—*are very constantly associated.* Tubal and interstitial nephritis cannot therefore be separated from one another by any distinct line of demarcation. They might be more correctly designated **acute** and **chronic** nephritis.

SUPPURATIVE NEPHRITIS.

Acute inflammatory processes in the kidney attended by the formation of pus, give rise to **renal abscesses.** Such processes, as already stated, often result obviously from the transmission by the blood-stream of infective particles from some primary focus, as in pyæmia, or they arise by direct extension from the lower urinary passages. In the latter they constitute what is commonly known as the "Surgical Kidney."

The abscesses met with in the kidney as the result of pyæmia are confined principally to the cortex, and resemble pyæmic abscesses in other organs. They are usually multiple, and are often surrounded by a thin zone of red hyperæmic tissue. Their size varies from a mere point up to that of a filbert. Their characters have been already described in the chapter on Embolism (p. 249).

SURGICAL KIDNEY.—This is the name commonly given to those inflammatory conditions of the kidney which result from obstructive and inflammatory diseases of the lower urinary passages. They occur frequently in association with renal and vesical calculus, obstructed ureter, urethral stricture, enlargement of the prostate, &c. These, and similar conditions, act upon the kidneys in three ways:—*

1. **By obstructing the outflow of urine from the pelvis.** Regurgitation from the bladder probably never occurs; but as a result of obstruction from any cause more or less of the full force of secretion acts upon the ureter, the pelvis, and the pyramids, and extends along

* The views here expressed are in accordance with the teaching of Marcus Beck. "Nephritis and Pyelitis consecutive to Affections of the Lower Urinary Tract," *Reynolds' System of Medicine*, vol. v.

the tubules to their closed ends. This chronic tension is a common cause of chronic inflammation. In cases of obstruction to the outflow from one kidney, the changes are limited to it.

2. **By producing circulatory changes in the kidney reflexly.** A close relation seems to exist between the deeper portions of the urethra, the prostate and the trigone, the parts upon which operations are performed, and the kidneys. An intense hyperæmia due to irritation of the nerves of these parts might in extensively diseased organs lead to arrest of the circulation and death from suppression of urine.

3. **By extension of decomposition from the bladder to the kidneys,** and irritation of the latter by septic products. As regurgitation does not occur, decomposition often remains long limited to the bladder. Extension perhaps takes place along ropy mucus lying as a cord in the opening of the ureter when this has become inflamed from other causes.

The changes in the kidney vary from the most chronic productive inflammation, to an acute suppurative process.

Simple long-continued increase of urinary pressure resulting from some obstruction to the flow of urine gives rise to chronic renal changes, which are characterised mainly by more or less cellular infiltration of the intertubular connective tissue. ("Interstitial Nephritis.") This cellular infiltration, which is exceedingly irregular in its distribution, occurs both in the pyramids and cortex. The tubules are in some parts found blocked with epithelium, whilst in others they are wasted or obliterated. The walls of the small arteries are not thickened. Owing to these changes, the kidneys are somewhat enlarged, the capsule is slightly adherent, the cut-surface paler than natural, and the consistence of the organs abnormally tough. As the process proceeds the pyramidal portions gradually become absorbed, the absorption commencing at the papillæ and extending until ultimately not only the pyramids but also the thickened cortex may

disappear, and the kidney be converted into a large cyst. If, on the other hand, the urinary obstruction be removed, the processes of inflammation and absorption may cease, and the indurated kidney will then become contracted.

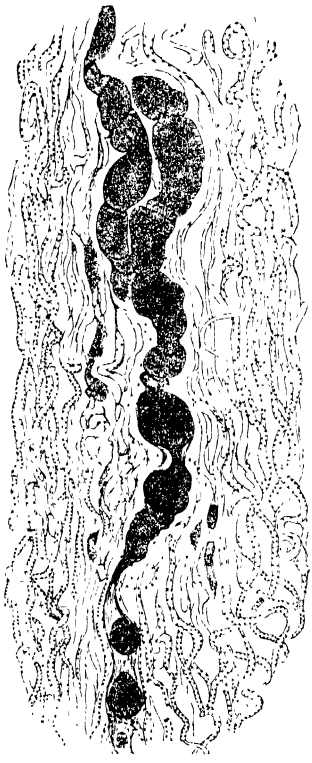
FIG. 123.

Surgical Kidney.—At the lower part of the figure is seen the cellular infiltration of the intertubular tissue, and the blocking of the tubes with epithelium and leucocytes. At the upper part, there is the commencing formation of an abscess. × 100.

In other cases, when the urinary obstruction is associated with inflammation of the lower urinary passages, the process is much more acute, the cellular infiltration of the intertubular tissue is much more abundant, and leucocytes accumulate in certain situations in such numbers as to give rise to abscesses. (Fig. 123.) The cortex of a kidney in such a case is thickened, soft, and pale as compared with the deep red pyramids; its consistence, however, will vary with the presence or absence of chronic interstitial changes. The capsule strips easily,

often tearing the substance a little, and exposing on the surface groups of yellow spots usually not larger than a lentil, and each surrounded by a red zone. Many of these contain a drop of pus. On section yellow streaks are often seen extending from the superficial lesions into the cortex; others exist in the pyramids. The pelvis is generally intensely inflamed.

FIG. 124.



Surgical Kidney.—Showing clouds of micrococci ascending along the tubules. Almost all nuclei have gone from their vicinity. They seem to have caused necrosis or degeneration of the tissues. × about 90.

Klebs described many of the tubules, even the convoluted, as crammed with micrococci. These seem to ascend from the pelvis along the tubules, distending them greatly and setting up irritative and degenerative processes along their line of passage. When stained with an aniline dye, the appearance shown in Fig. 124, from a specimen of Mr. Boyd's, is seen. It is extremely probable that these organisms are the cause of the suppuration. Though very often the urine in the pelvis of such kidneys is septic, it is not necessarily so.

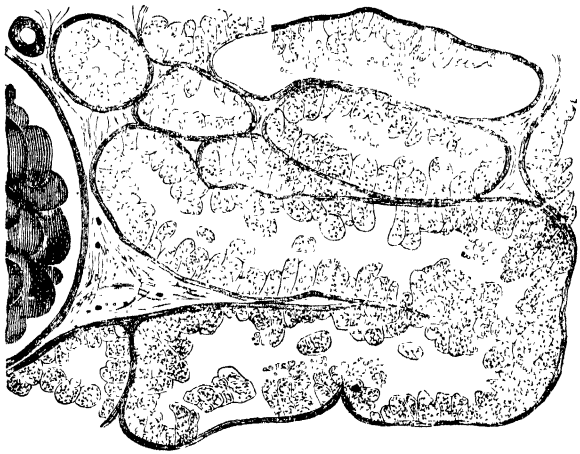
TUBAL NEPHRITIS.

Tubal, parenchymatous, or acute nephritis, is that subacute inflammation of the kidney which constitutes the more acute forms of Bright's disease—those which are characterised by a more or less marked beginning, scanty and highly albuminous urine, and dropsy. In its more advanced stages it is the large kidney of chronic Bright's disease.

The changes which take place in the kidney have their seat mainly in the cortex. They comprise increased vascularity and exudation into the urine tubes, with swelling, and, later, probably proliferation of the tubular epithelium. The prominence of the vascular phenomena, however, varies very considerably in different cases.

In the most acute cases of Bright's disease—those

FIG. 125.



Tubal Nephritis.—The earlier stage of the process. Showing the swelling of the tubular epithelium, and some exudation products in the urine tubes. In some of the tubes the epithelium has fallen out during the preparation of the section. × 200.

which are induced suddenly as from exposure to cold, the vascular changes are marked. In these cases the contraction of the cutaneous vessels and the check to the function of the skin caused by the chilling of the surface, lead to considerable hyperæmia of the organs. There is abundant exudation into the urine-tubes, many of the capillaries at the same time frequently rupture, and thus there is an escape of blood-corpuscles and of liquor sanguinis into the tubes of the cortex; hence the blood and "blood-casts" in the urine which are so characteristic of the early stages of these most acute forms of the disease. In this stage the process may quickly subside, and, with the exception of some swelling and desquamation of the tubular epithelium, no further alterations take place in the kidney.

FIG. 126.

Tubal Nephritis — a Single Urine Tube.—Showing the accumulation within the tube. In the few epithelial cells which have escaped, is seen the granular condition of the protoplasm. × 200.

In the less acute cases, those known as chronic Bright's disease with large kidney, the vascular phenomena are less marked, and changes in the tubular epithelium are more prominent. The epithelial elements become swollen and granular. (Fig. 125.) The granules, which are often so numerous as to occlude the nucleus of the cell, are soluble in acetic acid, and thus differ from molecular fat. This is the condition known as "cloudy swelling." Many small cells also are seen within the tubes, and these have been supposed to be the products of epithelial proliferation. It is probable that some of them are thus produced, although the majority must be regarded as having escaped from the vessels. Owing to these changes the tubes become distended with cellular elements. (Fig. 126.)

In addition to the cell-forms, many of the tubes also

contain hyaline cylinders, which are commonly regarded as consisting of coagulated substances which have escaped from the vessels. By many pathologists, however, this hyaline material is supposed to be the product of a mucoid, or some allied, metamorphosis of the epithelium. The cell-forms contained within the tubes adhere to this hyaline substance, and some of them are washed away and appear in the urine as "epithelial casts." A varying number of emigrant leucocytes also are usually found around the Malpighian tufts.

The alterations which these changes produce in the physical characters of the kidneys vary according to the extent of the hyperæmia. The organs are always considerably increased in size, and more or less abnormally vascular. The capsule separates readily, exposing a perfectly smooth but vascular surface. The consistence is diminished, the tissue breaking with a soft, friable fracture. On section, the increase in the size of the organ is seen to be principally due to the increased thickness of the cortex. This is either of a reddish-brown, or of an opaque-white or pale buff colour; these differences depending upon the relative proportion of blood and of accumulated intratubular elements. Although in the earliest stage of the most acute forms of the disease the colour is redder than natural, it usually soon becomes pale and opaque. This is owing to the swelling of the epithelial elements and to the accumulation in the cortical tubes. The blood becomes expressed from the intertubular vessels, and hence the increased vascularity is most evident in the Malpighian corpuscles, beneath the capsule, and in the pyramidal portions of the organ. The Malpighian corpuscles stand out as prominent red points, and the pyramidal cones are of a deep red colour, thus contrasting strongly with the pale opaque cortex.

The termination of the process varies. The increased vascularity and epithelial change may, as already stated, subside, and the inflammatory products passing away in the urine, the organ gradually returns to its normal con-

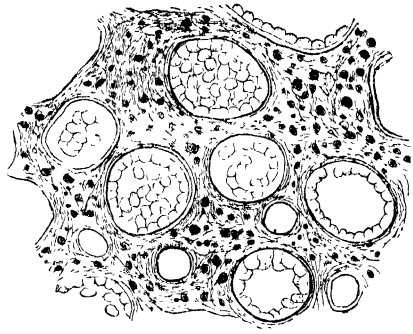
dition. In other cases the disease continues; and although the vascularity diminishes, the vitality of the epithelial elements become so much impaired that they undergo retrogressive changes. The cells then continue to come away with the urine, adherent to the casts, but instead of presenting the swelled granular appearance as in the earlier stage of the disease, they contain molecular fat. This fat gradually increases in amount as the degeneration proceeds, until ultimately the cells are destroyed, and it appears as free molecules and granules on the tube-casts.

This fatty degeneration of the epithelium is attended by corresponding changes in the appearance of the organ. The redness diminishes, and the Malpighian corpuscles are less prominent. The enlarged cortex presents a yellowish-white tinge, studded with minute yellowish streaks. This is owing to the presence of fat in the tubes of the cortex. This fatty stage, if only slightly advanced, may undoubtedly pass off. The degenerated cells are carried away by the urine, from those which remain in the tubes the fat is probably partially absorbed, the retrograde process gradually ceases, and the organ returns to nearly its normal size and condition. In other cases the degeneration continues, and, owing to the loss of epithelium, the kidney becomes somewhat diminished in size. This atrophy, however, I believe never occurs without changes in the intertubular connective tissue.

When the inflammatory process is of longer duration, or when the kidneys are the seats of repeated attacks of sub-acute inflammation, *the intertubular connective tissue invariably becomes involved.* This tissue becomes infiltrated with small cells which ultimately tend to form a fibrillated structure. (Fig. 127.) The new intertubular growth may gradually increase, and so lead to more or less irregular atrophy of the organ, such as will be described as occurring in interstitial nephritis. (See "Interstitial Nephritis.") In other cases death ensues before any

marked atrophy has taken place, and thus the organ may remain smooth and large to the termination of the disease. The intertubular growth is sometimes found thickly studded with fatty granules.

FIG. 127.



Tubal Nephritis.—Duration of disease, six months. Kidneys large; capsules, non-adherent; surface, smooth; tissue, soft.—Showing, in addition to the intratubular change, the cellular infiltration of the intertubular connective tissue. × 200.

SCARLATINAL NEPHRITIS.—The changes which take place in the kidney in scarlatina were formerly regarded as precisely similar to those which have been just described as tubal nephritis. Recent investigations, however, show that this view requires considerable modification. It has long been known that in scarlatina cases sometimes occur in which the kidney change differs from the type of ordinary acute nephritis; and such cases have been described by Prof. Klebs as **glomerulo-nephritis.** It is mainly, however, owing to the more recent researches of Dr. Klein that any exact knowledge of the scarlatinal kidney exists.* The changes as described by Dr. Klein may be thus briefly summarised:—

* "The Anatomical Changes of the Kidney and other Organs in Scarlatina of Man," by Dr. Klein: *Trans. Path. Soc. Lond.*, 1877, vol. xxviii.

The earliest changes—those occurring during the first week of the disease—comprise :—

1. Increase of the nuclei covering the glomeruli of the Malpighian corpuscles.

2. Hyaline degeneration of the elastic intima of minute arteries, especially of the afferent arterioles of the Malpighian corpuscles. This change produces a swelling of the intima, so as in some places to cause a distinct narrowing of the lumen of the vessel. The capillaries of the Malpighian corpuscles are in parts altered in the same way, in consequence of which many of them become impermeable.

These marked and early changes in the Malpighian corpuscles are important, as helping to explain those cases occasionally met with, in which death occurs from anuria and uræmia, and no catarrhal or other conspicuous alterations are found in the kidneys.

3. Multiplication of the nuclei of the muscular coat of the minute arteries, and a corresponding increase in the thickness of the walls of these vessels.

4. Cloudy swelling of the epithelium in the convoluted tubes, with multiplication of the epithelial nuclei. Granular matter and even blood may also be found in the tubes and in the cavity of Bowman's capsules. These parenchymatous changes are in the early stages of the disease but little marked.

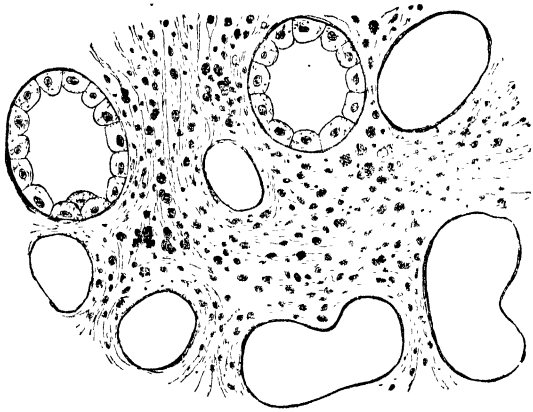
The later changes—those occurring after the first week—consist in :—

5. A cellular infiltration of the intertubular connective tissue of the cortex (interstitial nephritis), together with an increase in the epithelial changes, and a crowding of the tubes with small round cells (leucocytes). The cellular infiltration commences around the larger vascular trunks, whence it spreads rapidly into the bases of the pyramids, and especially into the cortex. As it increases, the epithelium undergoes fatty degeneration, and the urine-tubes gradually become obliterated.

INTERSTITIAL NEPHRITIS.

Interstitial or chronic nephritis is characterised by a gradual increase of the connective tissue of the kidney and by atrophy of the tubular structures. This, as has been seen, occurs in the more advanced stages of tubal nephritis (see Fig. 127); in scarlatinal nephritis; and also as a result of obstruction in the lower urinary passages. But it is most frequent, and constitutes the most prominent structural change in that most chronic variety of Bright's disease which is known as chronic Bright's disease with contracted kidney, and which is characterised clinically by insidious onset, increased secretion of urine

FIG. 128.



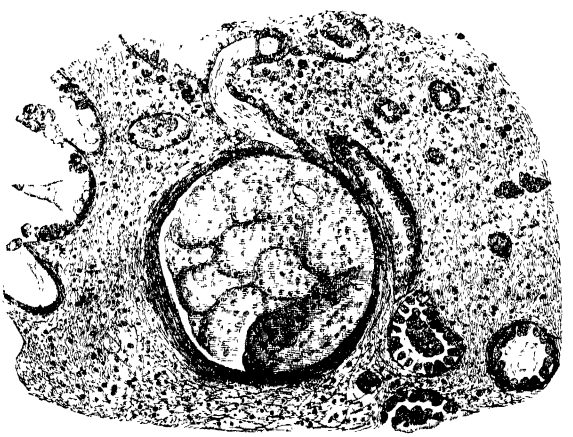
Interstitial Nephritis.—The earlier stage of the process. Showing the cellular infiltration of the intertubular connective tissue. The epithelium has fallen out of some of the tubes during the preparation of the section. × 200.

with the absence both of marked albuminuria and of dropsy. It must, however, be distinctly understood that no line of demarcation is to be drawn histologically between *inter-* and *intra*-tubular changes; or clinically

between the two varieties of Bright's disease. Intertubular changes are most marked as the result of long-continued irritation, and they therefore constitute the prominent histological feature in the most chronic forms of this disease.

In these most chronic cases the changes in the kidneys being so exceedingly gradual in their onset, are not preceded by any marked vascular phenomena or by any

FIG. 129.



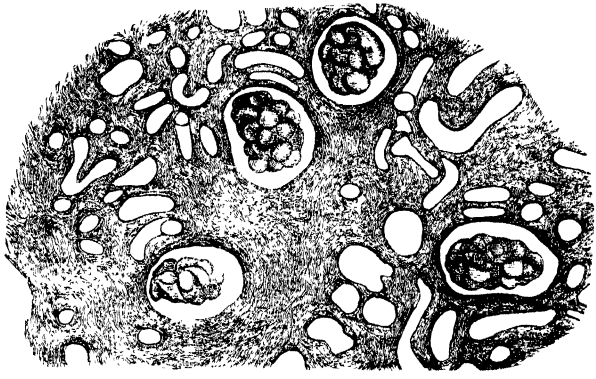
Interstitial Nephritis.—An advanced stage of the process. Showing the intertubular tissue with the granular and fatty débris which result from the degeneration. × 100.

alterations in the tubular epithelium. The first change appears to consist in some cellular infiltration of the intertubular connective tissue (Fig. 128); but usually owing to the chronicity of the process the cells are not numerous. The cortical portion of the kidney is principally involved, and although here the change is more or less general, the new growth is more abundant in some parts than in others, being usually most so around the Malpighian bodies and in the neighbourhood of the capsule, with

which it is closely united. In this stage the tubes and their epithelium are often unaffected.

In the early stage, the kidney may be of natural size, the capsule usually separates less readily than in health, and the surface of the organ is slightly granular. On section, the cortical substance is in some cases paler, in others redder, than natural. The cut-surface also looks obscurely granular; and the consistence of the kidney is

FIG. 130.

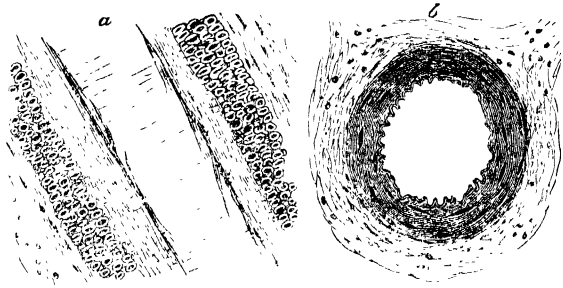


Interstitial Nephritis.—A very advanced stage of the process. Showing the large amount of tissue between the tubes of the cortex, and the extensive atrophy of the tubes. The degenerated epithelium which was contained in some of the tubes has fallen out in the preparation of the section. × 50.

usually slightly dense and tough. As the process proceeds the tubular structures gradually atrophy. This is probably mainly owing to the pressure exercised by the intertubular growth, and to the cicatricial contraction which it undergoes. The atrophy consequently is not uniform, but is more marked in some parts than in others. The tubes are now found in many parts diminished in size, or completely obliterated; whilst in others they are irregularly dilated, and filled with degenerated epithelial

products. Their walls are usually thickened. As the atrophy proceeds the intertubular tissue thus becomes mingled with the granular and fatty débris which results from the retrograde process. (Fig. 129.) The Malpighian bodies become approximated, and the secreting structure throughout large tracts of the kidney is destroyed. (Fig. 130.) The irregular pressure exercised by the new growth gives rise also to the formation of cysts. These originate partly in the Malpighian capsules, and partly in the urine-tubes—the latter becoming irregularly dilated.

FIG. 131.



Arteries from contracted Kidney of advanced Chronic Bright's Disease.—a. Longitudinal section, showing the great thickening of the circular muscular coat, also of the outer fibrous coat, and the internal connective-tissue layer. *b.* Transverse section of another vessel less diseased. Here is seen the thickening of the circular muscular and external fibrous coat. × 200.

The small arteries of the kidney also undergo important alterations. These were first described by Dr. Johnson. Dr. Johnson states that the walls of these vessels are thickened, owing to hypertrophy of their circular muscular fibres; this change is well represented in the accompanying drawing. (Fig. 131.) The external fibrous coat of the vessel is also thickened, and it appears to be continuous with the new intertubular tissue. This thickening of the external coat has been especially insisted upon by Sir W. Gull and Dr. Sutton. I have

usually found it associated with the muscular hypertrophy, which is undoubtedly the most prominent structural change. Similar changes occur in the vessels of other parts.

In this more advanced stage of the disease the kidney is diminished in size. Its surface is more granular, the capsule more thickened and adherent, and it cannot be removed without tearing the kidney substance. The superficial vessels are seen unduly marked in the depressions between the granulations. The cortex is tough and fibrous, of a reddish, yellowish-grey, or buff colour, mottled with yellow streaks and patches; and usually numerous small cysts are distributed throughout it. Calcareous deposits also are sometimes seen as white streaks between the tubes of the pyramids.

CHAPTER XLI.

INFLAMMATION OF THE LUNGS.

In the lungs, inflammatory processes comprise the three following principal varieties :—**Croupous, broncho-** or **catarrhal,** and **chronic** or **interstitial** pneumonia. Of these, the former occurs as an independent affection, whereas the two latter are usually the result of some antecedent bronchial or pulmonary inflammation.

CROUPOUS PNEUMONIA.

Croupous, exudative, or **lobar** pneumonia is that form of pulmonary inflammation which is met with in the disease known as Acute Pneumonia. This is now known to be a *general* disease of which the pneumonic consolidation is the prominent local lesion; and its clinical history suggests the probability of a specific organism as its cause. (See chapter on "Organisms.")

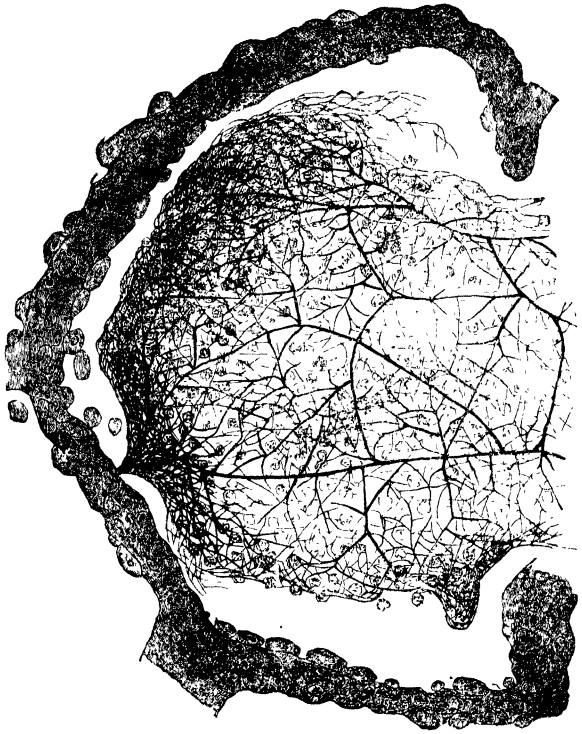
The local process is characterised by intense inflammatory hyperæmia of the lung, and by the exudation of a large amount of coagulable material into the pulmonary tissue. It is termed "croupous" by the Germans, from the supposed resemblance of the histological process to that of croup. The term "lobar" is applied to it because it almost invariably affects an extensive portion of the lung. The process is commonly described as consisting of three stages—1st, that of **engorgement**; 2nd, that of **red hepatization**; and 3rd, that of **grey hepatization.**

In the *first* stage, that of **engorgement,** the lung becomes exceedingly vascular, the changes in the blood-vessels and circulation being such as have been already described as characteristic of inflammation. The organ is of a dark-red colour, its specific gravity and absolute weight are increased, its elasticity is diminished, it is less crepitant and more friable than natural, and pits upon pressure. Its cut-surface yields a reddish, frothy, tenacious liquid.

In the *second* stage, that of **red hepatization,** there is an exudation of liquor sanguinis and migration of blood-corpuscles into the pulmonary tissue. Some of the vessels may also rupture, and thus small extravasations occur. The exuded liquids coagulate within the air-vesicles and terminal bronchioles, the coagulum enclosing numerous white and some red blood-corpuscles. (Fig. 132.) It is stated by some German pathologists that the coagulum is in part produced by certain changes in the epithelium like those believed to occur in croup. (See "Croupous Inflammation of Mucous Membranes.") The lung is now much heavier than in the preceding stage, and is increased in size, so as to be often marked by the ribs. It is quite solid, sinks in water, and cannot be artificially inflated. It does not crepitate under the fingers, and is remarkably friable, breaking down readily with a soft granular fracture. The cut-surface has a markedly granular appearance, seen especially when the tissue is torn. This is owing to the plugs of coagulated

exudation-matter which fill the alveoli. The colour is of a dark reddish-brown, often here and there passing into grey. This admixture with grey sometimes gives a marbled appearance. Throughout this stage there

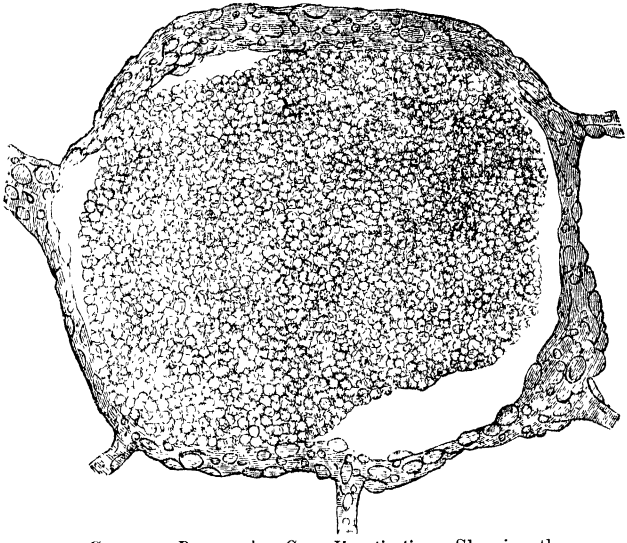
FIG. 132.



Croupous Pneumonia—Red Hepatization.—Showing the fibrinous coagulum in one of the pulmonary alveoli, enclosing within its meshes numerous leucocytes, which are already commencing to undergo fatty metamorphosis. A few leucocytes also are seen on the alveolar walls, and the alveolar epithelium is swollen and granular. × 200.

appears to be but little alteration either in the alveolar walls or in the alveolar epithelium. On the former are often seen a few leucocytes, and the latter is usually swollen and granular. (Fig. 132.) The pleura covering the solid lung always participates more or less in the inflammatory process. It is opaque, hyperæmic, and coated with lymph.

FIG. 133.



Croupous Pneumonia—Grey Hepatization.—Showing the large accumulation of cellular elements within one of the pulmonary alveoli, which in some parts have undergone such extensive fatty degeneration that their distinctive outlines are no longer visible. × 200.

The *third* stage, that of **grey hepatization,** is characterised by a continuance in the emigration of leucocytes, and by more marked changes in the epithelium. The white blood-corpuscles continue to escape from the vessels, their number within the alveoli gradually in-

creasing. The epithelial cells lining the alveolar walls become more swollen and granular. The pulmonary alveoli thus become completely filled with cells, so that the fibrinous exudation is no longer visible as an independent material, as it is in the stage of red hepatization. (See Fig. 132.) The fibrinous material now disintegrates, and the cells rapidly undergo retrogressive fatty changes, so that, as usually seen, the alveoli are filled with granular elements, which in many parts have lost their distinctive outlines. (Fig. 133.) The alveolar walls themselves, with few exceptions, remain throughout the process unaltered, although occasionally when this stage is unusually advanced they may be found, here and there, partially destroyed. The weight, density, and friability of the lung now become even greater than in the stage of red hepatization, although the granular aspect of the cut-surface is much less marked. The tissue is now quite soft and pulpy, and a puriform liquid exudes from its cut surface. The most prominent feature, however, is the alteration which takes place in the colour of the organ. This gradually changes from a dark reddish-brown to a grey or yellowish-white. This is owing partly to the pressure exercised upon the blood-vessels by the exuded substances and newly-formed cells, and partly to the fatty degeneration which the latter have undergone. The stage of grey hepatization, when far advanced, has been termed "suppuration of the lung."

Athough these three stages of the pneumonic process have been described as succeeding one another in orderly succession, it must be remembered that each stage does not occur simultaneously throughout the whole of the affected area of the lung. The changes advance irregularly, so that whilst one portion of the lung is in the stage of red hepatization, another may be in the grey stage—hence the mottled marbled appearance of the consolidation. The rapidity also with which the several stages succeed one another is subject to marked variations. In some cases the pneumonic consolidation very rapidly

becomes grey, whilst in others the time occupied in the transition is much longer.

The pneumonic process may terminate in the four following ways:—

1st. **In Resolution.**—The gradual return of the lung to its normal condition is the natural and much the most frequent termination of croupous pneumonia. This is effected by the fatty and mucoid degeneration of the inflammatory products which have accumulated within the alveoli, which thus become so altered that they can be removed by absorption; together with the return of the blood-vessels to a normal condition and the establishment of the circulation. Granular pigment, derived from the escaped red corpuscles, is often mixed with the softened matters, and appears in the expectoration. Where this process of resolution is taking place in the lung, the granular appearance of its cut-surface is completely lost; it is of a yellowish-grey colour, and a tenacious puriform liquid can be expressed from its substance.

2nd. **In Abscess.**—The formation of abscess is a rare result of pneumonia. Such a result appears to be favoured by a bad constitution, and by any circumstances which tend to impair the general health, especially the abuse of alcohol. The abscess is more common in the upper than in the lower lobes. Circumscribed gangrene of the lung also may occasionally terminate in abscess. This takes place by the expulsion of the necrosed tissue through the bronchi, and the formation of a layer of granulation tissue upon the walls of the cavity, which generates pus. The cavity may ultimately close by granulation and cicatrisation. These abscesses of primary origin are usually single, and thus differ from those due to pyæmia.

3rd. **In Gangrene.**—This, which is also rare, is most common in chronic drunkards and in those of debilitated constitution. Two conditions appear to be principally concerned in bringing about this result:—one is the in-

terference with the supply of blood by the extensive formation of coagula in the pulmonary and bronchial vessels, together with considerable hæmorrhage into the pulmonary tissue; the other is the injurious influence of septic inflammatory products. The gangrene is usually limited to a small area of the pneumonic lung, and is either diffuse or circumscribed.

4th. **In Chronic Pneumonia.**—If the inflammatory process does not subside, and the exuded substances are not absorbed, the alveolar walls gradually become involved. These become thickened by a new growth of fibro-nucleated tissue, and thus is produced more or less fibroid induration of the organ. (See "Interstitial Pneumonia.") This termination of croupous pneumonia is comparatively rare.

BRONCHO- OR CATARRHAL PNEUMONIA.

Broncho-, catarrhal, or **lobular** pneumonia is inflammation of the lung-tissue associated with, and usually secondary to, inflammation of the bronchial mucous membrane. In the earlier stage, the pulmonary inflammation is commonly limited to scattered groups of air-vesicles, hence the term **lobular** which is applied to it. As the process advances, the inflammatory nodules may gradually coalesce, so as to produce larger tracts of consolidation. The inflammatory products which fill the alveoli consist largely of cells derived from the epithelium of the alveoli and from the bronchial mucous membrane; exudation and emigration play a much less prominent part in the process than they do in croupous pneumonia. Owing to this preponderance of epithelial products, and to the association of the pulmonary with the bronchial inflammation, the process has been termed **catarrhal** pneumonia.

PATHOLOGY.—The pneumonic process, as already stated, is invariably associated with bronchial catarrh. In some cases, it would appear that the injury which produces

the bronchial inflammation produces at the same time inflammation of the air-vesicles, but much more frequently the bronchitis precedes the pneumonia, and gives rise to it in a manner to be hereafter described. Whatever causes inflammation of the bronchial mucous membrane may thus be a cause of broncho-pneumonia. Simple bronchitis, especially in childhood and old age, and also the specific bronchitis associated with measles and whooping-cough, are the most frequent precursors of the disease. All conditions which tend to impair the general health favour the occurrence of the pneumonia. They do so by rendering the bronchial mucous membrane abnormally liable to become inflamed, and also by diminishing the power of the respiratory muscles, and thus aiding in the production of pulmonary collapse.

Inflammation of the bronchial mucous membrane may give rise to broncho-pneumonia in two ways:—1st, by causing in the first place collapse of the lung-tissue; and 2nd, by the direct extension of the inflammation from the bronchi to the air-vesicles. Of these the former is much the most frequent. The pneumonic process being the result of the bronchitis, almost invariably involves both lungs.

1. Broncho-pneumonia consecutive to Collapse.—Collapse of the lung-tissue greatly favours the occurrence of broncho-pneumonia, and usually the pneumonic process is confined principally to those portions of the lung in which collapse has taken place. There are two circumstances chiefly concerned in the production of the collapse which is consecutive to bronchitis—the narrowing or occlusion of the bronchial tubes by the inflammatory swelling of the mucous membrane and the catarrhal secretion, and the weakness of the inspiratory power. The collapse thus induced is especially frequent in the posterior and inferior portions of the lungs—those portions in which, when confined to bed, the inflation of the lung is often least complete. Commencing here, the process may gradually extend upwards till large areas of

the lungs become involved. In other cases, owing to a more irregular distribution of the bronchial obstruction, the collapse is limited to small isolated portions of the lung. These portions vary in size from a hemp-seed to a walnut. They are commonly more or less wedge-shaped, with their apices toward the bronchus with which they communicate, and the lung-tissue around them usually presents various degrees of congestion and emphysema.

The tendency of the pneumonic process to occur in the collapsed portions of the lung is due partly to the hyperæmia which is induced by the collapse, and partly to the irritation of inhaled bronchial secretion. Collapse of the lung-tissue invariably induces more or less congestion. This is owing to the absence of the expansion and contraction of the air-vesicles which normally aid the pulmonary circulation, and also to the impediment to the blood-flow resulting from imperfect aëration. This congestion is quickly followed by œdema, and the bluish-purple, collapsed portions of the lung become darker in colour, less resistant, and more friable in consistence. In lung-tissue thus altered, more or less escape of liquor sanguinis and corpuscles, with swelling and desquamation of the alveolar epithelium, is prone to supervene.

Another circumstance which often appears to play a prominent part in the causation of the pneumonic process is the presence within the alveoli of the inflammatory products of the bronchial mucous membrane. These products are frequently found in scattered groups of air-vesicles, and they are evidently inhaled. (See Fig. 134.) They are found both in the air-containing and in the collapsed portions of the lung, but especially in the latter, the presence of collapse necessarily interfering with their removal by expectoration or absorption. These inhaled products are often found filling small groups of alveoli *without any evidence of subsequent inflammation*, and there can be no doubt that many of the patches of consolidation which are usually described as pneumonic are really non-inflammatory in their nature, and are thus

produced. At the same time, owing to the irritation of the inhaled secretion, it tends to induce inflammatory changes within the alveoli, and these changes are frequently largely owing to its presence.

2. **Broncho-pneumonia independent of Collapse.**—Although the pneumonic process is usually consecutive to collapse, it may occur independently. This may be owing either to the direct extension of the inflammation from the bronchi to the air-vesicles, or to the influence of inhaled inflammatory products. In other cases, it is possible that the injury which causes the bronchitis causes at the same time inflammation of the pulmonary alveoli.

HISTOLOGY, &c.—The appearances presented by the lungs after death vary. The bronchi are always more or less inflamed, and contain thick mucus. The lung-tissue exhibits, associated in various degrees, collapse, congestion, œdema, emphysema, and pneumonic consolidation. The bluish, non-crepitant, depressed portions of collapse, which become darker and more friable with age, are usually most abundant in the lower lobes and margins of the lungs. The collapse sometimes involves the whole of one lobe, but more commonly it is limited to smaller areas. When scattered and limited in its distribution, there is usually more or less emphysema of the intervening portions of the lung.

Those portions of the lung in which the pneumonic process has supervened most commonly appear as scattered nodules of consolidation, varying in size from a small pea to a hazel-nut. These are ill-defined, and pass insensibly into the surrounding tissue, which is variously altered by congestion, collapse, and emphysema. They are of a reddish-grey colour, slightly elevated, smooth, or very faintly granular, and soft and friable in consistence. As they increase in size they may become confluent. In a more advanced stage, the nodular and more diffuse consolidation becomes paler, firmer, drier, and somewhat resembles in appearance ordinary grey hepatization.

When examined microscopically, this consolidation is seen to consist of an accumulation within the alveoli of a gelatinous mucoid-looking substance, small cells resembling leucocytes, and epithelial elements. In many cases much of this accumulation is precisely similar to that contained in the smaller bronchi, and it is evidently the inflammatory and richly cellular bronchial secretion which has been inhaled. (Fig. 134.) It is also often partly

FIG. 134.

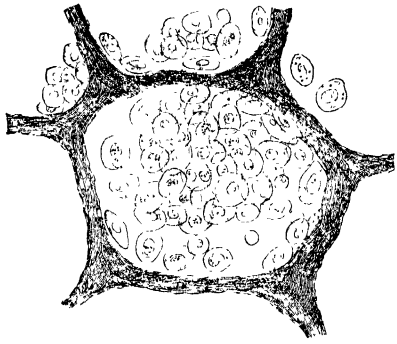
Broncho-Pneumonia.— From a child aged four, with capillary bronchitis. A section of one of the patches of consolidation. Showing the stuffing of the alveoli with what appears in the main to be inhaled bronchial secretion. × 200.

the result of exudation and emigration from the pulmonary capillaries; for, as shown by Cohnheim, blood-stasis so injures the walls of the blood-vessels that the blood-corpuscles and liquor sanguinis readily permeate them (see p. 213). Associated with this material are epithelial elements. These vary considerably in number. In some cases, and in some portions of the consolidation, they may be very few, whilst in others they may constitute the predominant change. (Fig. 135.)

The subsequent changes which take place in the lungs vary. When the disease does not end in death, resolu-

tion is the most common termination. The contents of the alveoli undergo fatty metamorphosis, and are removed by expectoration and absorption, the lung gradually regaining its normal character. This process, however, is less readily effected than in croupous pneumonia, and it often occupies such a lengthened period that some thickening of the bronchial and alveolar walls and dilatation of the smaller bronchi remains. In chronic cases this fibroid thickening is much more marked, and considerable irregularly distributed pig-

FIG. 135.



Catarrhal Pneumonia.—From a case of acute phthisis. Showing the large epithelial cells which fill the alveoli. × 200.

mented induration and bronchial dilatation may be produced. (See "Chronic Pneumonia.") In these chronic forms the contents of the alveoli sometimes caseate, and then become encapsuled, or in quite exceptional cases lead to disintegration.

HYPOSTATIC PNEUMONIA.—Allusion must be made here to a form of lung-consolidation which is often described as pneumonic, but which, in reality, is for the most part non-inflammatory in its nature. This is the so-called hypostatic pneumonia. This condition is met with

at the bases and most dependent portions of the lungs in the course of both chronic and acute diseases, and also in the aged and debilitated. It consists in the main of collapse, hyperæmia, and œdema of the lung-tissue, resulting from weak inspiratory power, feeble circulation, and gravitation. The consolidation thus mechanically induced is increased by more or less exudation of liquor sanguinis and blood-corpuscles into the alveoli, which exudation is due to the damage to the walls of the capillaries caused by the imperfect circulation.

INTERSTITIAL OR CHRONIC PNEUMONIA.

Interstitial or chronic pneumonia is characterised by a gradual increase in the connective tissue of the lung, which leads to an induration of the pulmonary texture, and to progressive obliteration of the alveolar cavities. It is commonly associated with catarrh and dilatation of the bronchi, and often with ulceration of the bronchial walls and excavation of the indurated lung.

PATHOLOGY.—It is exceedingly doubtful if interstitial pneumonia is ever a primary and independent affection. It probably in all cases owes its origin to some antecedent more acute inflammation of the pulmonary or bronchial textures, or of the pleura. It may be stated generally that all inflammatory processes in the lungs which become chronic lead to an increase of the connective-tissue elements, and consequently to a fibroid induration of the organs; and in this respect, therefore, these processes resemble similar ones in other parts—*e.g.*, in the liver, kidney, and mucous membranes. In the lungs, by far the most common cause of such induration is tuberculosis, and in all cases of phthisis, excepting in those which are the most acute, there is more or less fibroid growth. The most chronic cases of phthisis—those in which the fibrosis is the most marked—are, it must be admitted, histologically somewhat closely allied to some forms of interstitial pneumonia.

The two diseases differ, however, in this respect—that whereas much of the pulmonary consolidation of phthisis tends to undergo molecular death and disintegration, that of interstitial pneumonia exhibits no such tendency, any destruction and excavation of the indurated lung which may take place being due to secondary inflammation and ulceration commencing in the bronchial walls. In considering the pathology of interstitial pneumonia, therefore, it is necessary to exclude, in the first place, the

FIG. 136.

Chronic Bronchitis.—Showing the new growth of fibro-nucleated tissue around the bronchus *b*, and the way in which this tissue is invading the walls of the adjacent alveoli. *v*, A divided blood-vessel. × 100, reduced ½.

pulmonary fibrosis of chronic phthisis. (See "Pulmonary Phthisis.") Interstitial pneumonia must be separated also from that form of pulmonary induration which is produced by long-continued mechanical congestion (see "Brown Induration of the Lung"), and from those more localised indurations due to chronic bronchitis (Fig. 136), and to syphilis.

There appear to be four conditions which may give rise to interstitial pneumonia. These are as follows :—

1. **Croupous Pneumonia.**—The pulmonary consolidation of acute croupous pneumonia in almost all cases undergoes complete resolution. This resolution is usually effected rapidly, but occasionally it is more protracted. When protracted, the hepatized lung tends to become slightly indurated, owing mainly to thickening of the walls of the alveoli. This indurated hepatization differs but little in its physical characters from ordinary red and grey hepatization; it is simply somewhat firmer, more resistant, and less granular. In very exceptional cases this small amount of induration, commencing in the alveolar walls, may gradually increase, so as ultimately to give rise to that extensive fibrosis of the lung which constitutes what is usually known as interstitial pneumonia.

2. **Broncho-pneumonia.**—This is a somewhat more frequent cause than the preceding. The greater liability of this form of pneumonia to lead to pulmonary induration is to be accounted for partly by its longer duration and greater tendency to become chronic, and partly by the existence of bronchial dilatation with which it is so frequently associated. That bronchial dilatation is favourable to an indurative pneumonic process has been insisted upon by Dr. Wilson Fox.* The existence of this dilatation favours the persistence of the catarrhal and pneumonic process. The removal of secretion is rendered difficult, and the retained secretion tends to keep up and increase the irritative process both in the dilated bronchi and also in the pulmonary alveoli, and this persistence of the bronchial and pulmonary inflammation leads to fibroid thickening of the bronchial and alveolar walls. In this way areas of fibroid induration are produced, which, as the process extends, may ultimately involve large portions of the lung. The progressive tendency of the process is probably partly to be explained by the fact that

* Reynolds' "System of Medicine," vol. iii. Article, Chronic Pneumonia.

pulmonary fibrosis is a cause of bronchial dilatation, so that fibrosis once established, by inducing further dilatation of the bronchi favours the extension of the bronchial and pulmonary induration (Wilson Fox).

Under this head may be included also those cases of induration and ulceration of the lung which result from obstruction of a main bronchus—such as is produced by the pressure of an aneurism. Here the retained bronchial secretion sets up inflammatory changes in the bronchial and alveolar walls, which gradually lead to induration and ulceration of the lung.*

3. **Pleurisy.**—This, in exceptional cases, leads to the development of an interstitial pneumonia. It appears to be in those cases of pleurisy which are more or less chronic, and in which the effusion remains long unabsorbed, that such a result is most liable to occur. The induration of the lung thus induced is often, however, partial, consisting merely in some increase of the interlobular connective tissue, originating and extending inwards as dense bands from the thickened visceral pleura. In other cases, pleurisy gives rise to a much more general fibrosis.

4. **The Inhalation of solid irritating particles.**—This, which occurs in miners, potters, stonemasons, grinders, &c., is the cause of the fibrosis of the lung so common amongst these workmen. The continuous irritation of the inhaled particles induces a bronchial and alveolar inflammation, and ultimately a progressive fibrosis, with dilatation and ulceration of the bronchi. Such cases often become tuberculous.

HISTOLOGY, &c.—The appearances presented by the lung when the fibrosis is extensive and general are very characteristic. The organ is diminished in size; the tissue is smooth, dense, firm—in parts almost cartilaginous in consistence; and it is irregularly mottled with black pigment. The alveolar structure of the lung

* See case by Dr. Irvine, *Trans. Path. Soc. Lond.*, vol. xxviii. p. 63.

is in most parts completely destroyed, and on section the dilated bronchi are seen as numerous large openings scattered over its surface. The dilated bronchi frequently become the seats of secondary inflammatory processes, which may lead to ulceration and ultimately to extensive excavation of the indurated tissue; but there is a complete absence of any of those caseous changes which are so characteristic of phthisis. This secondary inflam-

FIG. 137.

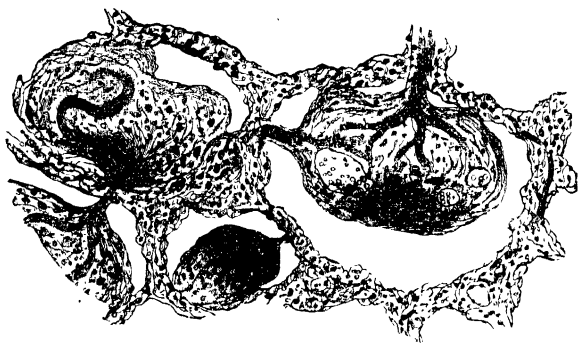
Interstitial Pneumonia.—From a case of so-called "cirrhosis" of the lung, in which the disease was unilateral. The bronchi were much dilated, and there was a complete absence of any caseous change. The drawing shows the new fibro-nucleated growth, both in the alveolar walls and in the interlobular tissue, also the pigmentation. At *a* a divided vessel is seen. × 100.*

mation of the dilated bronchi is induced by the irritating and often putrid secretion which they contain, and which is only with great difficulty completely removed by expectoration. The pleura is almost invariably considerably thickened and adherent.

* When this specimen is examined with a higher magnifying power a delicate reticulum can be seen between the cellular elements.

The histological changes may be described generally as consisting in the development of a fibro-nucleated tissue in the walls of the alveoli, in those of the bronchi, and from the interlobular connective tissue; which new growth, as it increases, and from its tendency to contract, gradually replaces and obliterates the alveolar structure. The character of these changes, however, varies somewhat according to the more acute inflammatory antecedents in which they originate. When the result of a croupous pneumonia, the primary, and usually the principal, change takes place in the walls of the alveoli (Fig. 137), although ultimately the interlobular tissue is involved. The alveolar

FIG. 138.

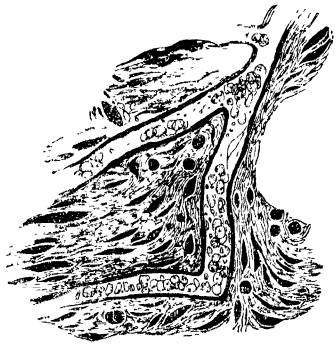


Chronic Pneumonia.—Vascularisation and fibroid development of intra-alveolar exudation-products. Blood-vessels are seen distributed in the exudation-products, which blood-vessels communicate with those in the alveolar walls. The alveolar walls are also thickened by a fibro-nucleated growth. × 100, and reduced ½.

walls become thickened by the growth of a small-celled tissue, in which, associated with the lymphoid cells, there are sometimes elongated fusiform cells such as are found in embryonic tissue which is undergoing fibroid development. The new growth in its earlier stages usually contains new blood-vessels, but later the tissue contracts,

and these become to a great extent destroyed. The alveolar cavities which are not obliterated, are either empty, or contain exudation-products or a few epithelial cells. In addition to the growth in the alveolar walls, I have met with three cases in which intra-alveolar exudation-products were undergoing fibroid development.* There was nothing peculiar in the macroscopical characters of the lungs, but the alveoli were found filled with a fibrinous meshwork and leucocytes somewhat similar to that met with in red hepatization. (See Fig. 132.) They differed, however, in this respect—that many of the cells

FIG. 139.



Chronic Pneumonia.—A portion of the intra-alveolar exudation-products (Fig. 138) more highly magnified. Showing the elongated spindle-cells, the fibrillation, and the blood-vessels containing blood-corpuscles. × 200.

were long and spindle-shaped, and blood-vessels were distributed amongst them, which blood-vessels communicated with those in the alveolar walls. (Figs. 138 and 139.) The alveolar walls also were thickened by a fibro-nucleated growth. It was therefore perfectly obvious that in these

* For one of these specimens I am indebted to Dr. Goodhart, who records the case in the *Trans. Path. Soc. Lond.*, vol. XXV. p. 33.

lungs the products of a previous acute croupous pneumonia were becoming vascularised and undergoing development into a fibroid structure, and that this intra-alveolar change was the principal cause of the fibroid induration of the organs.

When the fibrosis is secondary to an ordinary bronchopneumonia, or to that induced by the inhalation of irritating solid particles, the new growth also originates principally from the alveolar walls. Here, however, the growth in the earlier stages is less uniform, and the peribronchial and interlobular connective tissue play a more prominent part in the process.

CHAPTER XLII.

PULMONARY PHTHISIS.

By Pulmonary Phthisis is understood a disease of the lungs which is characterised by progressive consolidation of the pulmonary texture, and by the subsequent softening and disintegration of much of the consolidated tissue; the upper portions of the organs being, in almost all cases, the first to become involved.

Respecting the nature of the morbid processes which lead to this consolidation and disintegration of the lungs —various opinions have from time to time been held by pathologists, and this diversity of opinion exists to some extent even at the present day. According to the older views, which were based upon the teaching of Laennec, phthisis was regarded in all cases as a **tuberculous** disease. Tubercle was looked upon us a non-inflammatory growth which was characterised by the caseous degeneration which it invariably underwent, and this caseous metamorphosis was held to be such a distinguishing peculiarity of the growth, that all caseous masses came to

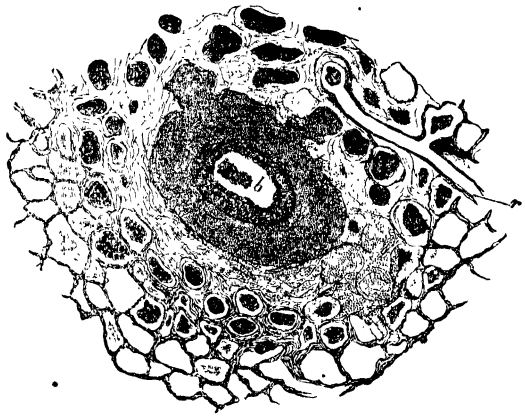
be regarded as tuberculous, and phthisis, in which caseation plays such a prominent part, was consequently regarded as a tuberculous disease. The various consolidations of the pulmonary tissue were described as "infiltrated tubercle," and tubercle in some form or other was regarded as so essential a constituent of the disease, that "phthisis" and "pulmonary tuberculosis" came to be synonymous terms. When the application of the term "tubercle" became limited by Virchow and his followers to the grey granulation, it was evident that these views were no longer tenable, and many, in accordance with the advocacy of the late Professor Niemeyer, regarded phthisis as due to a form of caseous pneumonia, which was quite independent of tubercle, although this growth might occur as a secondary and accidental complication. It was then said that some cases of phthisis were tubercular, and that others were not; and attempts were made to subdivide the disease into distinct pathological varieties —such as "tuberculous," "pneumonic," and "fibroid" phthisis. Our present knowledge of tuberculosis necessarily involves considerable modification of these older views. Before considering the pathology, however, it will be well to study the histology of the disease.

HISTOLOGY.—The histological changes in the lungs which occur in pulmonary phthisis are similar to those which are met with in these organs in acute miliary tuberculosis. They differ mainly in this respect—that whilst in the latter disease these changes are usually limited to small areas (hence the miliary character of the lesions), in the former they commonly involve much wider tracts of tissue. Phthisical consolidation is, however, **lobulated** in its distribution. This is owing to the fact that the injury causing the inflammation is inflicted through the medium of the bronchi. (See "Etiology.") This lobulated distribution of the consolidation is exceedingly characteristic, and even in those acute cases, in which, owing to the rapid and extensive implication of the lung, the consolidation may to the naked eye appear

almost uniform (like croupous pneumonia), the microscope will usually reveal a lobular character. (Fig. 140.)

The structural changes met with in the lungs in phthisis are mainly of four kinds :—1st. An accumulation of epithelial cells within the pulmonary alveoli; 2nd. The presence within the alveoli of a fibrinous exudation and leucocytes; 3rd. A cellular infiltration and thickening of the alveolar walls, together with, in most cases, a similar change in the walls of the terminal bronchioles; and 4th. An increase in the interlobular connective tissue. These four kinds of morbid change are very constantly associated, although in very different degrees; and some of

FIG. 140.



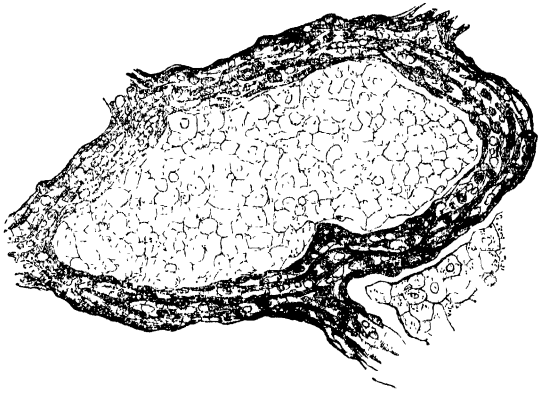
Acute Phthisis.—A transverse section of a terminal bronchus (air-passage) and the surrounding alveoli.—Showing the *lobulated* character of the pulmonary consolidation. *b*, cavity of bronchus containing a little mucus. *v*, a blood-vessel. × 50, reduced ½.

them are more prominent and characteristic than others. The preponderance of one or other of them produces those variations in the physical characters of the lungs which are met with in the different stages, and in the

different varieties of the disease. These various structural changes must now be considered separately, together with the more important alterations in the physical characters of the organs which they respectively produce.

1st. **An accumulation of epithelial cells within the pulmonary alveoli.**—This is one of the most frequent changes met with in phthisis, and is precisely similar to that which has been already described as occurring in cases of catarrhal pneumonia. (See Fig. 135.) The alveoli are found filled with large nucleated elements,

FIG. 141.

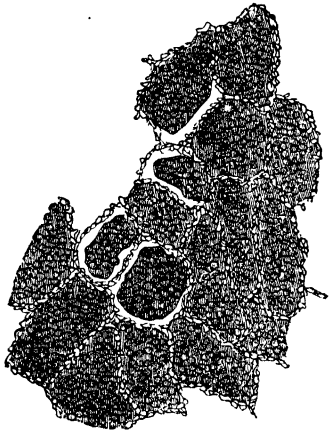


Acute Phthisis.—Showing one of the alveoli filled with epithelial elements, and marked cellular infiltration of the alveolar wall. × 200.

which are the offspring of the epithelial cells normally lining the alveolar walls. (Fig. 141.) In some acute cases of phthisis this alveolar accumulation may constitute almost the only morbid change, and although there is always some cellular infiltration of the alveolar walls, the great bulk of the pulmonary consolidation is due to the stuffing of the alveolar cavities with catarrhal products. (Fig. 141.) In some parts—those in which the

change is the most recent—the large cells which fill the alveoli and the alveolar walls will be found but little altered, but in the greater portion of the consolidated tissue the cells will be seen in various stages of retrogressive metamorphosis, and the alveolar walls destroyed; whilst in those tracts of tissue in which the process is most advanced, all trace of structure is lost, and nothing

FIG. 142.



Section of Lung from a Case of Acute Phthisis.—Showing that the consolidation consists almost exclusively of products accumulated within the alveoli. In some parts a free space is seen between the alveolar walls and their contents; this is due simply to the shrinking of the latter caused by the hardening of the specimen. × 50.

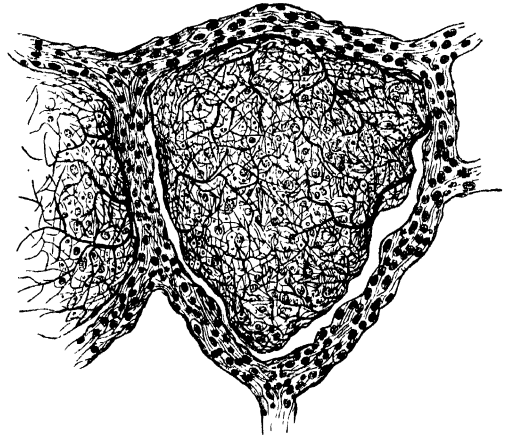
is seen but a granular débris. These changes are precisely analogous to those met with in many of the larger nodular lesions of acute tuberculosis. (See Figs. 93 and 94.)

2nd. **The presence within the alveoli of a fibrinous exudation and leucocytes.**—This is less frequent than the preceding. (Fig. 143.) The exudation-products are similar to those which fill the alveoli in ordinary croupous

pneumonia. (See Fig. 132.) The coagulum, however, is usually not so abundant, neither is the fibrillation quite so distinct. In the most acute forms of phthisis this may constitute the principal cause of the pulmonary consolidation, but commonly it is associated with more or less epithelial proliferation.

The appearances presented by the lungs in those cases in which the pulmonary consolidation is mainly due to the *intra*-alveolar changes above described are very characteristic. The consolidated tissue is quite soft and

FIG. 143.



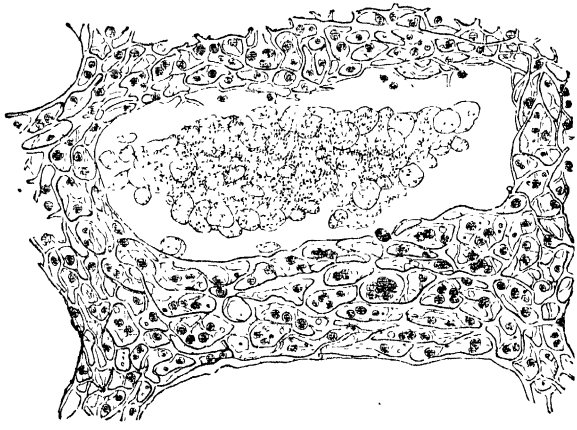
Acute Phthisis.—Showing one of the alveoli filled with fibrinous exudation and leucocytes, and some cellular infiltration of the alveolar wall. × 200.

friable, breaking down very readily under the finger, and there is a complete absence of any induration. The consolidation, although sometimes almost uniform, usually presents a somewhat lobulated outline, indicating the implication of different groups of the pulmonary lobules (p. 425). The colour varies from a reddish to a yellowish grey, and scattered through the consolidated mass are

often small portions of a more decidedly yellow tint. These latter correspond with those parts in which the retrogressive changes are the most advanced, and they are even softer in consistence than the surrounding tissue. In many parts the consolidated tissue will be found broken down, so as to form cavities of various sizes. These usually possess irregular walls, which are quite soft and friable, like the solid tissue which surrounds them.

3rd. **A cellular infiltration and thickening of the alveolar walls,** together with, in most cases, a similar

FIG. 144.



Section of Lung from a Case of somewhat Chronic Phthisis. —Showing the thickening of the alveolar walls by a fibro-nucleated adenoid-like tissue; together with an accumulation of epithelial cells within the alveolar cavity. The latter are undergoing retrogressive changes. × 200.

change in the walls of the terminal bronchioles.—This is very constantly associated with the former intra-alveolar changes, and it must be regarded as the most characteristic phthisical lesion, although its extent varies very considerably in different cases. The change is precisely similar to that which has been already described as

occurring in acute miliary tuberculosis. In its earlier stages a few small lymphoid cells are seen infiltrating the alveolar septa, which are thus slightly thickened. (See Figs. 141 and 143.) As the change proceeds, the number of these cells increases, and from them an imperfect fibro-nucleated structure is developed (Fig. 144.) This structure contains no new blood-vessels. As this new tissue develops in the alveolar walls, it gradually obliterates and replaces the alveolar cavities, so that whilst in some portions the thickened alveoli may be found still containing epithelial elements, exudation products, or even giant-cells, in others large tracts will be seen, consisting almost entirely of the small-celled growth. The development of this new non-vascular tissue in the alveolar walls leads to the partial, or even complete, obliteration of the pulmonary capillaries, which, as will be seen subsequently, constitutes an important element in the causation of the retrograde changes.

The changes which may subsequently take place in this alveolar growth vary. The infiltrated septa may rapidly break down before any marked thickening or development of new tissue has had time to occur; whilst in other less acute cases there is a considerable development of the imperfect fibro-nucleated tissue, which, although it may remain as a more or less permanent structure, usually owing to insufficient vascular supply, undergoes in its turn retrogressive metamorphosis. These two kinds of change are very often found taking place simultaneously in different portions of the consolidated lung. In those portions in which the new tissue is undergoing degeneration, it, together with the cells which may be contained within the alveoli, will be seen to have become converted into a structureless granular débris, whilst perhaps in the immediate vicinity of these degenerated portions will be found a more permanent fibro-nucleated structure.

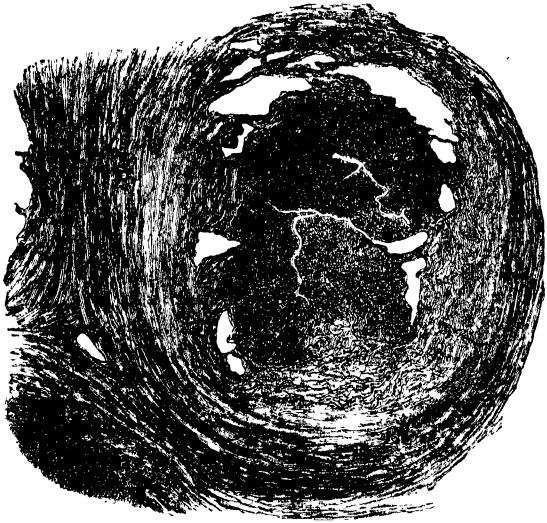
Respecting the alteration which the growth of this small-celled tissue produces in the physical characters of

the lungs—it may be stated generally that it usually leads to more or less induration of the pulmonary texture. The extent of this induration, however, will vary according to the characters of the new tissue. If the tissue be almost entirely cellular, such as is the case when it is very rapidly developed, it will produce but little, if any, induration of the pulmonary consolidation, which, consisting mainly of the intra-alveolar accumulations, will be soft and friable in consistence, much resembling that which has been already described. When, on the other hand, as is more frequently the case, there is any considerable development of the imperfect fibro-nucleated growth, or its reticulum is dense and abundant, there will be a corresponding induration of the consolidated tissue. In many cases these changes produce uniform tracts of indurated consolidation of a greyish colour mottled with black pigment, in which there may be scattered here and there yellowish patches corresponding to those portions which have undergone retrogressive fatty changes.

4th. **An increase in the interlobular connective tissue.**—This is met with, to a greater or less extent, in all the more *chronic* forms of phthisis. This tissue, which surrounds the bronchi and blood-vessels, and contributes to the formation of the alveoli, is found not only increased in amount, but also altered in character. In the earlier stages of its development, when it contains numerous small cells, although many parts of it may resemble the growth in the alveolar walls, its structure is more like that met with as the result of chronic indurative processes in other organs. It has a much greater tendency to become developed into a fibroid tissue than the alveolar growth, and is rarely the seat of those retrograde changes which are so frequent in the tissue originating in the alveolar walls. As usually met with, it consists either of wavy fibres or of a more or less reticulated structure, with a varying number of round, spindle-shaped or branched cells. (Fig. 145.) Associated with it, in most cases, are granules of black pigment. These

differences in the pathological tendencies and structure of the alveolar and interlobular growths are mainly owing to differences in the amount of their vascular supply. Whereas in the former the vessels become obliterated in the manner already described, in the latter this obliteration is much less complete or entirely wanting. In the

FIG. 145.



Chronic Phthisis.—Shewing the new interlobular fibroid growth surrounding and encapsulating a degenerated and caseous portion of the consolidated lung. × 50, reduced ½.

most chronic cases of phthisis this interlobular growth may constitute the predominant structural change, and large tracts of the pulmonary texture may be found completely replaced by it. (See "Interstitial Pneumonia.")

An increase in the interlobular connective tissue in phthisis—inasmuch as the new tissue has so marked a

tendency to become dense and fibroid—leads to extensive induration of the pulmonary texture; and further, owing to the contraction which the tissue tends to undergo, its growth ultimately produces a corresponding contraction of the diseased lung. In all those cases of phthisis in which there is either a marked thickening of the alveolar walls, or an increase in the interlobular connective tissue, any cavities which may exist in the consolidated and indurated tissue are characterised by the tough and fibroid character of their walls, these presenting a marked contrast to the soft friable tissue which surrounds the cavities in those cases in which the pulmonary consolidation is mainly due to intra-alveolar changes.

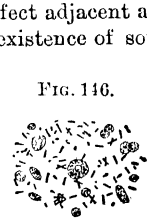
Changes in the Bronchi.—Allusion must now be made to certain changes in the bronchi. These tubes are invariably more or less involved in pulmonary phthisis. Some catarrh of the bronchi is constantly present in phthisical lungs. The catarrh is sometimes general, but much more commonly it is limited, and more strictly confined to such portions of the lung as are becoming, or have already become, consolidated. In many cases there is a marked tendency of this bronchial catarrh to lead to extensive cellular infiltration of the deeper structures of the bronchial wall. This is especially the case in the scrofulous. (See "Scrofulous Inflammation," Fig. 103.) This cellular infiltration sometimes leads to the production of small ulcers. These have thickened opaque edges, and when once formed they tend to increase. In addition to these changes in the bronchial mucous membrane, there is often a cellular infiltration of the peri-bronchial tissue, and here small nodules of new growth are frequently met with—especially around the smallest bronchi.

PATHOLOGY.—Having thus briefly described the various structural changes met with in the lungs in phthisis, it remains to consider the nature of the morbid processes upon which they depend. In the first place, it is evident that these changes are analogous to those which have been seen to occur in the several forms of pulmonary

inflammation. The fibrinous exudation and leucocytes, and the accumulation of epithelial cells within the alveoli in croupous and catarrhal pneumonia, with, in the more chronic cases, the ultimate infiltration of the alveolar walls; and the increase in the interlobular connective tissue which characterises the interstitial process, closely resemble the phthisical lesions. These considerations, together with those derived from the study of the etiology of the disease, are sufficient to justify the conclusion that the morbid processes which lead to the consolidation and subsequent disintegration of the lung come within the category of **inflammation,** and that the differences in the histological changes to which they give rise are mainly due to differences in the intensity and duration of the inflammatory process.

But although phthisical consolidation of the lung is the result of inflammation, it is obvious from our previous considerations (p. 290), that the process does not owe its origin to simple causes. The *progressive* character of the inflammation, and its tendency to infect adjacent and distant portions of the lung shows the existence of some continuous irritant; and for some years past it has become increasingly probable that this consists in the presence of some **pathogenic organism.** Koch appears to have discovered the organism. His, and all subsequent investigations, tend to show that the Bacillus tuberculosis is invariably present both in the lungs and in the sputum in all cases of phthisis (Fig. 146); and we must therefore regard phthisis as a more or less chronic **pulmonary tuberculosis** (pp. 307–8).

FIG. 146.



Tubercle Bacilli.—In phthisical sputum. × 300.

In considering the causes of the differences in the histological changes in the lungs, it is important to bear in mind what has been already stated respecting the

variations in the character of the textural alterations in inflammation which are produced by differences in the intensity and duration of the inflammatory process. When studying the process of inflammation it was seen that the most intense forms of the process were characterised by abundant fluid and corpuscular exudation; whereas in inflammations of less intensity and longer duration, tissue-formation played a prominent part. These textural changes also varied according to the intensity of the inflammation. In the least severe and most chronic forms these changes tended to be limited to the elements immediately adjacent to the blood-vessels and lymphatics, whereas in inflammations of somewhat greater intensity more distant elements became involved. Further, whereas in the former case these changes usually resulted in the formation of a small-celled tissue which tended to become fibroid, in the latter, the more distant elements—being in most cases incapable of further development—tended to undergo retrogressive changes. In the lungs, the truth of these propositions was borne out by the differences which were seen to exist in the histological characters of the lesions in the various forms of pulmonary inflammation, and also in acute tuberculosis.

If the pathology of these inflammatory processes in the lungs be kept in view, the explanation of the differences in the histological characters of the lesions in pulmonary phthisis becomes evident. In those cases in which the inflammatory processes are of slight intensity and of long duration, the most marked structural change will consist in the development of a small-celled growth in the alveolar walls and in the interlobular tissue—a growth which tends, more or less, to become developed into a fibroid structure; whereas in those cases in which the inflammation is of greater intensity, fluid and corpuscular exudation, and proliferation of the alveolar epithelium, will constitute more prominent parts of the process.

The intensity of the inflammatory process not only determines the histological characters of the pulmonary consolidation, but also to a great extent, the subsequent changes which take place in it. In those cases of phthisis in which the intensity of the inflammatory process is considerable, not only do the epithelium and exudation-products which have accumulated within the alveoli quickly degenerate and break down, but any small-celled tissue which may have been developed in the alveolar walls or around the terminal bronchioles also softens and dies, and thus the vitality of large tracts of the pulmonary consolidation may become destroyed. In those cases, on the other hand, in which the process is less intense, the small-celled growth produced in the alveolar and bronchial walls is more permanent, and there is an increase in the interlobular connective tissue. It is these two kinds of change, the one tending towards death, and the other towards the production of new tissue, which produce the caseation and softening on the one hand, and the induration on the other, which, associated in such various degrees, make up the diverse physical characters of the phthisical lung.

These various secondary changes which may take place in the pulmonary consolidation of phthisis must be considered more fully. They are of three kinds—resolution, development into an imperfect fibroid tissue, and retrograde metamorphosis.

Resolution.—Much of that consolidation of the lung which is the most rapidly induced, and which is consequently owing to the presence of intra-alveolar exudation matter, may become absorbed. The resolution of the consolidation may thus be complete, or after the absorption of the intra-alveolar products there may remain more or less infiltration of the alveolar walls.

Fibroid Development.—This, as has been seen, may take place in the growth in the alveolar walls, and also in the new interlobular tissue. The tissue which originates in the walls of the alveoli, however, being for the most

part destitute of blood-vessels, is incapable of forming a very mature structure, although it may develop into an imperfect tissue, which may remain for some time permanent, and so contribute to the induration of the lung. In the new interlobular tissue there is not the same interference with the vascular supply, and hence this forms a much more fully developed and permanent structure, and it is the principal source of the pulmonary fibrosis. The extent of this fibrosis is, for the most part, in direct proportion to the chronicity of the disease.

Retrograde Metamorphosis.—It is this kind of change which leads to that caseation, softening, and disintegration which is so characteristic of phthisis, and which distinguishes phthisical from other forms of pneumonic consolidation. A retrograde change in the inflammatory products is an invariable accompaniment of acute non-phthisical pneumonia. Much of the exudation matter and epithelium which fill the alveoli undergoes fatty and mucoid changes, and as the circulation becomes restored in the pulmonary capillaries, the degenerated products are absorbed, and the lung remains intact. In phthisical consolidation, however, this removal of the inflammatory products does not take place. The contents of the alveoli degenerate, but the degenerated products are not absorbed, and the consolidated lung undergoes a rapid or gradual process of disintegration.

In studying the causes of this retrograde metamorphosis, which constitutes so essential a feature of the disease, we find that it is due principally to conditions interfering with the circulation. Of these conditions, that which probably occupies the most prominent place is that cellular infiltration of the walls of the alveoli and smaller bronchi which is such a constant though very variable factor in phthisis. It has been seen that this infiltration is especially characteristic of scrofulous inflammations, and that it occurs in a modified form in those who are not markedly scrofulous, and also in all pulmonary inflammations which become chronic. When the infiltra-

tion is marked, and especially when rapidly induced, the effect of the pressure which the young cells exercise upon the pulmonary capillaries is to obstruct the circulation, and so not only to prevent the absorption of any intra-alveolar products, but also to lead to necrotic changes.

Amongst other conditions which tend to interfere with the circulation, and so to cause necrosis, must be mentioned, as obtaining in the most acute forms of phthisis, the pressure which is exercised upon the pulmonary capillaries by the inflammatory products which have accumulated within the alveoli; and that tendency to stagnation of the blood-stream which is an invariable accompaniment of every intense inflammation. A destruction of the capillaries by the tubercle bacillus possibly constitutes a factor in the process.

In addition to the interference with the circulation, an important element in the causation of the retrograde changes of phthisis is probably that inherent weakness of the lungs (usually inherited), which not only renders them especially susceptible to injury, but also, when injured, renders them abnormally incapable of recovering from the inflammatory process which has been induced.

In many cases of phthisis also, especially in the more chronic forms, secondary inflammation and ulceration of the pulmonary consolidation, resulting from the injurious influence of retained secretions and inflammatory products, contributes to the destruction of the lung.

ETIOLOGY.—In studying the etiology of phthisis it is obvious, in the first place, that accepting the tubercle bacillus as an essential element, something more is necessary for the production of the disease. The bacillus, as has been seen, must in some situations be constantly entering the lungs by means of the respired air (p. 397)—in hospitals set apart for the treatment of consumption the source of infection must abound, and yet how exceedingly rare are the instances in which the development of phthisis results. The other necessary factor is

something inherited or acquired—**inherent in the individual.**

The influence of **hereditary predisposition** is so marked that it must necessarily occupy a prominent place in the pathology of phthisis. As to the nature of what is transmitted—although in quite exceptional cases this may possibly be the tubercle bacillus—speaking generally it is in all probability simply a tendency to disease. It may be said that this tendency consists in some feebleness of the constitution in general, and often of the lungs and other organs in particular. As a result of this feebleness there is usually a want of constitutional vigour, the power of resisting injurious influences is diminished, and the lungs and often other organs and tissues which are especially weak are in consequence abnormally liable to become inflamed. Further this inherited weakness not only renders certain organs abnormally liable to inflammation, but also abnormally incapable of recovering from the effects of the inflammatory process; and there is thus more or less tendency to retention and accumulation of inflammatory products. (See "Scrofula.")

Another important factor in the development of phthisis is the state of the **general health**. Quite apart from any inherited constitutional feebleness there can be no doubt that an impaired state of health greatly favours the development and progress of the disease. It is when *both* these obtain that we have the most favourable conditions.

In these two conditions, therefore, hereditary predisposition and state of general health, we have the other factor—the something inherent in the individual which appears to be necessary for the production of phthisis. It is this **inherent** condition which must be regarded as constituting a soil favourable to the development of the inspired bacillus, and, whatever it may be, its importance is difficult to over-estimate.

So little is at present known of the life-history of Bacillus tuberculosis that the circumstances which favour

its growth cannot be formulated; but in endeavouring to understand the favourable influence inherent in the individual in the case of phthisis, we shall probably find some explanation in the **apical distribution** of the pulmonary lesion.

The causes of this apical distribution are probably to be sought for in the diminished range of respiratory movement which obtains in the highest portions of the lungs. As a result of this diminished movement, there is diminished aeration of blood, and, in certain conditions of health, a tendency to stagnation of the blood-stream in the pulmonary capillaries. The stagnation of the circulation leads to more or less injury of the walls of the vessels, and a slight leakage is thus induced.

It is obvious that any inherited or acquired weakness must favour the occurrence of these apical changes. General feebleness and want of vigour lead to loss of muscular strength and weakness of the heart, and thus tend to prevent the full expansion of the chest, to cause a stooping posture of the body, and to impair the blood- and air-circulation—all conditions favouring blood-stagnation in the highest portions of the lungs. Further—the toneless condition of the blood-vessels, and the poverty of the blood with which the constitutional feebleness is so often associated, furnish the conditions which are the most favourable to transudation. May not the existence of such physical conditions in the highest portions of the lungs, if not essential to, at all events greatly favour, the injurious influence of the inspired bacillus? And may we not, by treatment which tends to obviate them, do much to prevent the development of phthisis?

CHAPTER XLIII.

INFLAMMATION OF THE BRAIN AND SPINAL CORD.

Inflammatory processes in the nervous centres are less frequent than was formerly supposed. Many of the morbid changes in the brain and spinal cord attended by softening and formerly regarded as the result of inflammation, are now known to arise from simple interference with the blood-supply, such as results from thrombosis, embolism, or degenerative changes in the walls of the blood-vessels. (See "Cerebral Softening.")

Inflammation of the brain and spinal cord may begin upon the surface, being secondary to an inflammation of the meninges, or it may commence in the substance of the organs. Sometimes the process is diffuse, sometimes circumscribed. It may run either an acute or a chronic course.

MENINGITIS.—This may arise by direct extension from other parts, especially the petrous bones around the middle ear; or it may be due to wound (septic) or to injuries without wounds such as blows, and especially exposure to great heat. It may constitute the specific lesion of an infective disease (epidemic cerebro-spinal meningitis); or it may appear as a secondary lesion in the courses of other infective diseases, as acute rheumatism, pyæmia, erysipelas, typhoid, &c. It may also be due to the presence in the membranes of abnormal bodies, particularly tubercle (p. 310).

In these cases a serous, fibrinous, or purulent exudation occupies the sub-arachnoid space, occurring in greatest abundance where this space is largest—*i.e.*, in the inter-peduncular space, the region of the anterior perforated spot, and the grooves of the sulci. Whilst tubercular meningitis affects chiefly the base, that from sunstroke

and the infective forms are most marked upon the convexity of the brain. The spinal meninges are as a rule less affected than the cerebral. The velum interpositum is often inflamed, leading to effusion of fluid into the ventricles; the ependyma thickens and becomes rough on the surface. The brain-substance generally is hyperæmic, often œdematous and soft; immediately beneath the inflamed membrane the congestion is marked, small hæmorrhages are common, and the grey matter more or less infiltrated with cells. The extent of the brain-changes corresponds with the extent and duration of the meningeal inflammation.

The above are generally acute diseases; but *chronic* inflammations occur from alcoholism, in general paralysis, syphilis, and other diseases, leading to circumscribed thickenings of the membranes, adhesions of the membranes, and superficial sclerosis of the subjacent brain- or cord-substance.

ENCEPHALITIS AND MYELITIS.—Inflammations commencing in the substance of the brain or spinal cord are, as a rule, circumscribed; but in the cord it is not uncommon for myelitis to extend through a considerable length of the grey matter. Mechanical injury causing contusions and lacerations is a common cause of inflammatory round-celled infiltration; so also is pressure, as is best seen in the neighbourhood of tumours, tubercular masses, parasites, &c., and in angular curvature of the spine. Cases occur also, especially in the cord, in which the cause of the inflammation is obscure. According to Charcot, hæmorrhage into the cord is generally the result of myelitis. Suppuration in the cord is extremely rare; in the brain it is more common, though still rare. In this situation the ordinary causes of abscess are three:—(1) Direct injury to the head, sometimes of a slight kind and unaccompanied by wound, but generally fracturing the skull, producing a wound and even leaving a foreign body in the brain-substance. (2) Disease of the skull-bones, especially of the petrous part around the middle ear. In

these cases the membranes and brain may all be adherent to the diseased bone, and the abscess lie close to the surface; or the abscess may lie deeply in the substance of the brain and produce no disturbance of the membranes. (3) Pyæmia: The abscesses in these cases, which are rare, are often multiple.

The process of inflammation in the brain is the same as elsewhere. It begins with hyperæmia, often accompanied by minute extravasations of red corpuscles; the tissue becomes infiltrated with leucocytes and considerably softened, so that it washes away under a stream of water too gentle to affect the healthy substance. At first uniformly red or mottled, the softened tissue gradually acquires a brownish or brownish-yellow colour, owing to changes in the hæmoglobin. The nerve-fibres, nerve-cells, and cells of the neuroglia become fatty and disintegrate; the fat-granules are taken up by leucocytes, which grow into large very granular cells, called "inflammatory" or exudation-corpuscles, or corpuscles of Gluge. (See Fig. 15.) The above process is described as **Inflammatory Softening**, and is quite distinct from the degenerative softenings from embolism, thrombosis, &c. (p. 69).

If the cause is of such a nature as to lead to suppuration, cell-infiltration increases greatly, replacing the normal structure; then the centre of the mass dies, and a yellowish or reddish pus forms. Such an abscess may spread until it bursts either externally or into the ventricles, and if it be opened during this stage its walls will be found shaggy, very vascular, dotted with hæmorrhages, and softer than normal; whilst, microscopically, all the stages of inflammation—from suppuration downwards—would be seen. But the abscess may at any time cease to spread, and become surrounded by a capsule of connective tissue, whilst the pus often undergoes mucous degeneration, and becomes thick and viscid. It is thought that pus thus encapsuled may dry up and caseate or calcify, or be even completely absorbed, leaving

little more than a scar. Abscesses may occur in any part of the brain, but are most common in the temporo-sphenoidal lobes.

SCLEROSIS OF THE BRAIN AND SPINAL CORD

Many diseases are characterised by the presence of excess of fibrous tissue in different parts of the central nervous system, such excess being accompanied by degeneration and atrophy of the proper nervous elements. The abnormal tissue is just such as results from a productive inflammation (p. 275), and many pathologists regard these diseases as of inflammatory origin. There is, however, much room for doubt in many cases, and other observers prefer to look upon the increase of connective tissue as due to a hyperplasia of the neuroglia, the cause being unknown. As lesions of this nature produce *induration* of the parts affected, they are called **Scleroses.** In their early stages, however, which are rarely seen, *softening* rather than induration results.

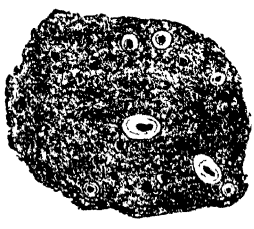
Sclerosis may be either **primary** or **secondary**—*i.e.*, the fibroid overgrowth may first appear, and by its pressure cause atrophy of the nerve-tubules; or the primary lesion may be that rapid degeneration of nerve-fibres which follows their separation from the cells of which they are processes, the fibroid overgrowth being consequent upon this. These changes may affect either the brain or the cord, and may be more or less diffuse in distribution, or limited to physiological tracts, such as the crossed and direct pyramidal; or small patches may be irregularly scattered through the part—disseminated or insular sclerosis. Either the grey or white matter may be the primary seat of the lesion, but in certain diseases the overgrowth generally extends from the one into the other, whilst in others such extension hardly ever occurs.

Naked-eye Appearances.—In the earliest stage a soft red patch, with more or less swelling, may indicate the seat of disease; but much more commonly the area is pale and greyish, its translucency and firmness varying

with the relative proportions of cells and fibrous tissue present. The part may be swollen, of normal size, or contracted; and the pia mater is generally more or less adherent. Often, however, no naked-eye change can be detected in the fresh cord. This should always be cut into portions about half an inch long, kept together by the membranes on one side, and placed in bichromate of ammonia (2 per cent). This stains the normal nerve-tissue greenish-brown, whilst the sclerosed tracts remain pale yellow, and are easily detected and traced. In sections, the altered tissue stains deeply with carmine. This is owing to the fact that the white substance of the nerve-fibres does not stain, but the connective tissue stains deeply. Hence the degree of staining is valuable as indicating, even to the naked eye, the degree of the sclerosis.

Microscopical Appearances. - In the cord it is almost always possible to compare the diseased with healthy tracts. We then find, as a rule, that in the *white matter* the clear rings (substance of Schwann), which normally surround the axis cylinders, have disappeared in the former, few if any axis cylinders being visible in it, and the connective tissue has increased so as to more or less completely replace the lost medullary substance. (Fig. 147.) In rarer cases leucocytes are found infiltrating the patch, and exudation-corpuscles may be numerous. The walls of the blood-vessels (external coats) also are said to be thickened. In the *grey matter*, intense hyperæmia is present in the early stages, and more or less round-celled infiltration. This is succeeded by fibroid overgrowth such as the above. The nerve-cells may be swollen at

FIG. 147.



Sclerosis of Spinal Cord — From a case of Progressive Muscular Atrophy. A transverse section. Showing the atrophy and disappearance of the nerve-fibres, and the new tissue between them. × 200.

first, but later on they are shrunken, often pigmented and diminished in number; and not uncommonly, the anterior cornu may be wholly destitute of them.

SCLEROSIS OF THE BRAIN.—This is less common than sclerosis of the cord, both as a primary and as a secondary lesion. *Primary* scleroses of particular parts have not been associated with definite symptoms. The overgrowth may be general, but is usually disseminated. It is found in many cases of insanity, but most constantly in general paralysis of the insane, which is believed to be due to sclerosis of the grey matter of the cortex, which later extends into the white substance. It is frequent also in isolated convolutions, in the pons, and medulla of epileptics and idiots. As a *secondary* lesion, a band of descending degeneration is found after destructive lesions of the motor fibres anywhere below the cortical centres. Such lesions are most common in the basal ganglia, especially the corpus striatum.

SCLEROSIS OF THE CORD.—In this part of the nervous system, certain symptoms are associated with sclerosis of certain tracts. This may be primary or secondary, and may affect either white or grey matter.

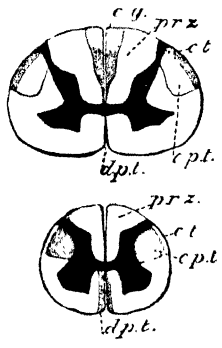
White matter.—Perhaps the best example of **primary** sclerosis of white matter occurs in locomotor ataxy. In this disease the naked-eye and microscopic appearances above given are found in the posterior root zone (Fig. 148, *p.r.z.*) (in-coordination), and are almost always most marked, or present solely, in the lumbar region. Commonly the sclerosis involves also the mesial portions of the posterior columns, and on the other hand the posterior nerve-roots and cells in the posterior cornu (lightning pains and anæsthesia). It may extend even to the lateral columns, causing paralysis. The process slowly extends up along the posterior root zone; very rarely it may be most marked in the dorsal or cervical region.

Idiopathic lateral sclerosis is another example, the lateral columns being affected as in the descending

degenerations soon to be described. The sclerosis tends always to extend to the grey matter. **Disseminated sclerosis** also occurs in the cord, the symptoms varying greatly with the spots affected. An annular sclerosis sometimes results from meningitis in caries of the spine.

The **secondary** degenerations of the cord are frequent and important. They are divided into **descending** and **ascending**—the former affecting centrifugal tracts (motor), the latter centripetal (some kind of sensory). The motor tract runs from the motor cortical centres through the corpus striatum and thalamus, down the crus and through the pons into the medulla. Here most of it crosses in the decussation to the opposite lateral column of the cord (crossed pyramidal tract, Fig. 148, *c.p.t.*), but a varying number of fibres run down along the anterior median fissure in the anterior column of the same side (direct pyramidal tract, *d.p.t.*). These latter probably keep on passing to the opposite side through the anterior commissure, and the fasciculi have generally disappeared in the lower dorsal region. The crossed tract extends to the lower end of the lumbar enlargement. Removal of the motor cortical centres, on one side, will therefore cause degeneration of the whole motor tract springing from it; and lesions lower down will cause degeneration of the portion of the tract

FIG. 148.



Secondary Degeneration — Section through the cervical and lower dorsal region of a cord destroyed by a fracture below the mid-dorsal region. The upper shows the ascending degenerations in the column of Goll and the cerebellar tract; the lower, the descending degenerations in the lateral and anterior columns. *c.g.* Column of Goll. *p.r.z.* Posterior root zone. *c.t.* Cerebellar tract. *c.p.t.* Crossed pyramidal tract. *d.p.t.* Direct pyramidal tract.

below them, more or less complete according to the number of fibres they damage. The tendency of this secondary lateral sclerosis to extend into the grey matter is much less than that of the primary, and atrophy of muscle is proportionately rarer.

Ascending lesions affect the columns of Goll (Fig. 148 *c g.*) and the cerebellar tract (*c. t*); the former extends the whole length of the cord, the latter comes to the surface about the second or third lumbar nerve, and runs upwards. In two cases (Gowers' and Hadden's), bands of ascending degeneration have been seen on the surface of the lateral column anterior to the cerebellar tract.

The difference between the two sets of lesions is that the cells which govern the nutrition of the motor fibres are at their upper ends (cortical cells, fourth layer?), whilst those which govern the nutrition of the sensory fibres are situate at their lower ends, in the grey matter of the cord (posterior cornu and Clarke's column?). The sketches (Fig. 148) were taken from a case of fractured spine a little below the mid-dorsal region, in which the patient lived seven months; they show the ascending and descending degenerations well. Statements vary as to the time at which the degeneration becomes apparent:—Bastian says 7–14 days; Schiefferdecker found that in dogs it began after 14 days, was well-marked after 4–5 weeks, but no sclerosis was noted until the eighth week (Ross, vol. i. p. 844).

Knowing the extent of these tracts, it is easy to see what secondary degenerations will result from a given lesion.

Grey Matter.—The great ganglion-cells of the anterior cornu are those which usually suffer primarily. They may be affected in large areæ, and *acutely*, as in infantile paralysis and the acute spinal paralysis of adults, in which groups of muscles or all the muscles of one or more limbs become paralysed; extension may occur for a short time, but as a rule it soon ceases. In the general spinal paralysis of Duchenne a similar lesion occurs less acutely, affecting as a rule the cells connected with the lower

limbs first, and spreading in the course of weeks or years to all the voluntary muscles, affecting them in groups and causing rapid wasting of them. The process may also be *chronic*, spreading slowly, not affecting large groups of cells, but a few at a time, so that individual muscles waste progressively, fibre by fibre, and paralysis comes on slowly—as in progressive muscular atrophy. It is, however, right to say that these lesions have not been found in all cases of this disease, and it is believed by many that the disease may have also a peripheral origin, being probably allied to cases of Duchenne's pseudo-hypertrophic paralysis, in which central lesions have but rarely been found.

In describing sclerosis of the white columns, we have already mentioned that the disease often secondarily involves the grey matter—*e.g.*, in tabes dorsalis and lateral sclerosis. Again, it is a common mode of ending in these diseases for the sclerosis to extend to the medulla, and destroy the cells of the all-important nuclei situate there. These nuclei suffer also primarily in glosso-labio-laryngeal paralysis.

In conclusion, it is necessary to remind the student that it is hopeless to attempt the diagnosis of the seat of nervous lesions without an accurate knowledge of anatomy and of nerve-physiology. With regard to the cord, the following facts will be found useful :—

The **antero-lateral columns** convey motor impulses from the cerebral cortex to the cells of the anterior cornu by means of the direct and crossed pyramidal tracts. Other fibres (anterior root-zone) are believed to have a looped arrangement, connecting cells of the anterior cornu at different levels, and probably aiding in co-ordination. The function of the cerebellar tract is unknown. Lesions of these columns offer impediments to the passage of cerebral impulses, and cause tremors, paresis, paralysis; or, if irritant, rigidity or spasm.

The **posterior columns** consist of the fasciculi of Goll or posterior median columns of which the function is un-

known, and of the posterior root-zone. The latter contains, in the lumbar region at least, afferent fibres of ordinary tactile sensation, and others which convey impressions of temperature and pressure and of muscular sense; also sensory fibres from the sexual organs. Interference with these columns will produce inco-ordination (from loss of muscular sense), diminution of sexual desire, and other obvious results.

With regard to the **grey matter**—the cells of the **anterior cornu** are motor. Destruction of them causes paralysis of the muscles they supply, followed by rapid atrophy of the nerves and of the muscles. The cells of the **posterior cornu** are concerned in sensation and especially in the transmission of **painful** impressions. The grey matter of the cord contains also many centres—*e.g.*, the oculo-pupillary in the cervical and upper dorsal regions; vaso-motor centres throughout the cord; centres governing the peristalsis of the alimentary tube; others preserving the tone of the sphincters vesicæ and ani; others in the lumbar region superintending micturition, defæcation, erection, ejaculation of semen, and parturition. All that is known of these centres is that they are not in the anterior cornu (Ross) for lesions of these cells do not affect them. Ross believes that the visceral centres are in Clarke's column, the cells here being bi-polar like those of the sympathetic, and the tract existing only in the dorsal and upper lumbar regions where visceral nerves are given off. The head of the columns is the nucleus of the vagus, the chief of visceral nerves. These centres may all be affected by lesions.

The **posterior root** conveys sensory impressions: lesions of it will produce anæsthesia, dysæsthesia, hyperæsthesia, pain, &c. The **anterior root** conveys motor impressions: lesions of it will cause tonic or clonic spasms, paresis or paralysis with rapid atrophy of nerve and muscle beyond.

Reflexes are of two kinds—**superficial** or **cutaneous**, **deep** or **tendon-reflexes**. The latter are probably stretch-

contractions, not true reflexes; but they occur only under conditions favourable to reflex action. In every reflex an afferent and an efferent nerve, together with a centre, are concerned. In disease reflex excitability may be increased or diminished. It will be increased by anything which lessens the resistance to the passage of the stimulus. Excitation of the cornual cells by strychnia has this effect, so, too, has removal of cerebral influence, as by sleep or disease of the lateral columns. It will be diminished by obstruction to the stimulus:—as by sclerosis of the posterior root-zone invading the nerve-roots or destroying the posterior cornual cells, or by damage to the anterior cells or nerve-roots; by some sedative drugs, as bromide of potash; or by increased cerebral control, as by an effort of the will.

CHAPTER XLIV.

REGENERATIVE PROCESSES IN TISSUES.

Destruction of tissue-elements has frequently been described in earlier chapters as the result of necrotic and various degenerative and inflammatory processes. It must now be briefly stated how such losses are repaired. It has already been said (p. 15) that cells of one embryonic layer always produce cells of tissues originally developed from that layer; and it is apparently true also that true regeneration of a tissue occurs only from cells of that tissue—muscle from muscle, epithelium from epithelium. Any form of connective tissue may, however, give rise to any other form—areolar tissue, bone, cartilage, &c. With regard to the origin of these tissues from leucocytes—the latter must, when we consider their sources, be considered as connective-tissue corpuscles.

The regenerative processes which may go on in adult mesoblastic tissues, are still imperfectly known. Their

reproductive energy has been supposed to be limited to molecular repair. But it is certain that the cells of most adult tissues retain the power of multiplication, though it may not be manifest under normal conditions. This is probably owing to the facts that the blood-supply they receive is sufficient only to maintain them in *statu quo*, and that the resistances opposing growth, such as pressure within the tissue, are now equal to the force with which they tend to multiply.

So far as investigation has yet gone, the nuclear figures, described at p. 13, have been found in each tissue to form the first stage of division of cells.

As no extensive regeneration occurs without the formation of new vessels, it may be well first to state what is known concerning their production.

VESSELS.

The formation of new vessels has been studied chiefly in the tadpole's tail, in sections of healing wounds, and in teazed preparations of granulation tissue. At the end of the second day after the infliction of a wound, and later, pointed processes, which are at first solid, are seen projecting from the walls of capillaries; they increase in length and anastomose with similar processes from other capillaries, or with processes of branched connective-tissue corpuscles. At first very fine, the processes gradually widen and become hollow, and thus an anastomosing set of vessels is produced. At this time a few nuclei are seen in their walls, the result of division of the original cell-nuclei, but nitrate of silver does not show the lines of union of individual endothelial cells. These develop subsequently. The process corresponds with that observed in the embryo (with the exception that no red corpuscles form in the cells), and is the same in the healing of wounds, in new growths, and in reproduction of lost parts.

Two much less certain modes of origin of vessels are described. (1) In granulation tissue, Thiersch states that

lymph-streams issuing from the vessels form channels between the loosely connected cells, which ultimately communicate with vessels, and fill with corpuscles. Observations of B. Hirschfeld support this view. (2) Spindle-cells in granulation tissue are said so to arrange themselves as to form canals which communicate with vessels. It is probable that they are really collected round a bud from a vessel (Ziegler).

As in the embryo, the new vessels may increase in size with the demands made upon them, muscular and fibrous coats being formed by cells which apply themselves around the original tube.

Adult vessels may increase greatly in size and thickness, as is seen in the gravid uterus and collateral vessels of a limb in which the main trunk has been tied; such vessels generally become tortuous as well as wider. Increased flow through the vasa vasorum is always present.

COMMON CONNECTIVE TISSUE.

This is the most frequent seat of new formation of all kinds—hypertrophy, tumour formation, and regeneration. With regard to the latter, it seems that loss of substance is made up for from two sources:—the fixed connective-tissue corpuscles and wandering leucocytes. Formerly all new cells in the tissues were regarded as products of connective-tissue corpuscles. Then it was thought that adult connective-tissue corpuscles were incapable of growth, and that almost all new fibrous tissue was of inflammatory origin, and hence many pathologists regard all scleroses as inflammatory. Now the happy mean seems to have been reached, and it is held that both connective-tissue corpuscles and leucocytes may form fibrous tissue. The difficulty in estimating the part played by each is extreme; but Senftleben's experiments (p. 267) on the cornea prove the regenerative power of connective-tissue cells, and Ziegler's experiments with glass chambers (p. 276) seem to demonstrate with equal

clearness the development of white blood-corpuscles. Some authors are inclined to think that scar-tissue of inflammatory origin is only temporary, being slowly replaced by tissue resulting from the regenerative processes going on in the neighbouring connective-tissue cells. The denser kind of connective tissue results as a rule from inflammation.

HEALING OF WOUNDS.

The union of most wounds and the repair of losses of substance are effected by the formation of more or less scar-tissue—*i.e.*, by the development of new vessels and new connective tissue. Several modes of healing are described, but they are fundamentally the same. They are—(1) Immediate union; (2) Union by first intention; (3) Healing by second intention or by granulation; (4) Healing under a scab; (5) Union of two granulating surfaces.

Immediate Union.—Described by Macartney in 1838, the occurrence of the process has been confirmed by Paget and Thiersch, who states that it occurred in wounds inflicted on the tongues of animals. The union is said to be effected by a blending of the practically unchanged surfaces of the wound, no lymph intervening as a bond. It is complete in twenty-four hours, and no scar results. Most pathologists deny that such a process ever occurs. They believe that lymph, possibly only in microscopic quantity, invariably forms the first bond of union. With them the next form is the speediest mode of healing possible.

Union by First Intention.—This generally occurs in well-treated incised wounds. It is prevented if the surfaces are not accurately brought together, being left gaping superficially or separated in their deeper parts by foreign bodies, blood or fluid exudation in any quantity; by movement of the surfaces on each other; by sloughing of the surfaces; or by irritation of any kind which excites inflammation going beyond the fibrinous stage. When these conditions are avoided by careful arrest of

rhage, cleansing, drainage, apposition, provision for rest, and prevention of septic and infective inflammations, the following changes take place:—The capillaries become thrombosed up to the nearest collateral; in tied or torsioned vessels the changes described at p. 234 set in. The injury inflicted by the knife was severe but strictly localised, and of very short duration. It excites free exudation of fluid and corpuscles. At first there are many red corpuscles in the discharge, but they rapidly diminish, and the fluid becomes clear and deep yellow. The discharge escapes between the edges of the wound if it is small in quantity, or through channels purposely left if large. The fibrin contained in the exudation coagulates on the opposed surfaces binding them together; it contains more or fewer leucocytes. It is this lymph, which forms the glaze on wounds left open. The exudation diminishes greatly as the effect of the injury is recovered from. Microscopic examination, after 24—36 hours, shows the edges of the wound separated by a narrow band of small round cells; the tissues close to the incision are swollen and hazy, and more or less infiltrated with leucocytes. New vessels develop after the second day, and shoot across from side to side, converting the lymph into granulation tissue (p. 275). This then goes on to the development of a scar (p. 277). The number of leucocytes about the wound varies with the amount and duration of the irritation; in some cases it is quite difficult to make out what holds the edges together. Thus in a herniotomy wound examined on the fourth day, the line of incision was recognised almost solely by the fact that the fat on one side was adherent to the deeper layer of the cutis on the other; the two seemed to be in actual contact, and there was hardly any round-celled infiltration. The part taken by the tissue-elements in scar-formation is not yet determined. The older a scar is the more closely does it resemble the normal tissue.

Union by Granulation.—When a wound cannot be brought together, or when union by first intention is

prevented, this form will occur. Until union takes place a raw surface is necessarily exposed to some irritation. This, some think, keeps up a constant exudation of fluid and leucocytes from the new vessels, just as the original injury excited such exudation from the vessels of the normal tissue. The leucocytes imbedded in a little intercellular substance become vascularised into granulation tissue. Others say that after the primary severe irritation has subsided, granulation tissue is produced by multiplication of the neighbouring connective-tissue corpuscles. However formed, the tissue increases in amount, either by continued infiltration with leucocytes or by multiplication of its own cells, or by both processes, until the wound is filled up to the level of the surface, when the granulations skin over, as described on p. 284. A granulating wound under ordinary dressings suppurates more or less freely, but one treated antiseptically and protected from irritation by the antiseptic employed, discharges a serous fluid. A section through granulation tissue shows on the surface a layer of small round cells with bi- or tri-partite nuclei, imbedded in a substance which is actually fluid superficially—this layer is breaking down into pus. Deeper are found fibro-blasts (p. 276), and deeper still, scar-tissue in all stages of formation. The thickness of the surface-layer, and the amount of pus formed, vary with the irritation to which the tissue is subjected. In some cases destruction equals or exceeds growth of granulations. Here again, therefore, treatment should be directed to the avoidance of all unnecessary irritation.

Healing under a Scab.—In this form the exudation is small in amount, and dries into a scab. It is not common in man except in superficial abrasions. Formation of granulation- and scar-tissue occur beneath it, as also does the inward growth of epithelium. When "skinning over" is complete, the scab drops off. The dry scab is but slightly irritant in itself, and it does not putrefy. When ulceration spreads beneath a scab, some infective agency

is probably the cause. The process of scab-formation is sometimes imitated by closing wounds, often leading to cavities, with collodion; or allowing blood or tincture of benzoin on lint to dry and occlude the opening. Such treatment is, however, dangerous; for if septic or infective organisms have entered and excite inflammation, the absence of drainage will be most prejudicial.

Union of Two Granulating Surfaces.—When two surfaces have granulated as above described, they may be brought together; and frequently the two surfaces will blend, thus saving the time which would be required for filling up from the bottom. Free suppuration and imperfect drainage will prevent such union. This is the way in which abscesses should heal when their walls are allowed to fall together by evacuation of the pus.

ADIPOSE TISSUE.

This is merely connective tissue, of which the cells are infiltrated with fat. Newly formed connective-tissue cells may certainly thus become infiltrated; but inflammatory tissue as a rule remains free from fat.

CARTILAGE.

A wound or breach in cartilage is generally repaired in the first instance by scar-tissue, which may be replaced later by hyaline cartilage formed from the perichondrium and by proliferation of neighbouring cartilage-cells, the matrix being formed, according to Strasser, from the protoplasm of the cells. Often this replacement by cartilage does not occur. In cases of fractured rib-cartilage the fibrous tissue may ossify into a clasp of bone round the broken ends.

BONE.

The regenerative power of bone is considerable, and depends chiefly upon the periosteum, to a less extent

upon the marrow. The process is best illustrated by the repair of a simple fracture.

During the first twenty-four hours an examination shows the broken ends of the bone lying in a collection of blood coagulated where it is in contact with the tissues, but fluid round the fracture. The bone ends are sharp and jagged, the periosteum more or less torn and stripped off, the medulla more or less deeply ecchymosed. The injury to the vessels of the part excites exudation of fluid and of cells; the latter infiltrate the torn tissues, so that in three or four days they are found to have lost their characteristic appearance, being soft, pink, and gelatinous, as is best seen in the medulla. In fact, they are granulating, and the granulation tissue increases in amount until the blood around the fracture has disappeared, and the ends of the bones are embedded in a mass of soft tissue. Not only do the periosteum and medulla give rise to this, but also other injured soft parts. From the third or fourth day certain large angular cells are seen close to the bone, which play the part of osteoblasts. Here, as elsewhere, the source of the cells of the granulation tissue, after the effect of the primary injury has subsided, is disputed; some referring their origin to leucocytes, others to the cells of the medulla and periosteum. This soft tissue is found in plenty about the tenth day, when it is difficult to distinguish the periosteum, which is swollen and infiltrated with cells like other parts. Now, the granulation tissue becomes firmer, and at about the fourteenth day the periosteum can again be seen covering a spindle-shaped swelling, which extends beneath it for some distance up and down the bone. As Billroth says, the ends of the bone are stuck into this spindle-shaped mass as if it were soft sealing-wax; there is a ring outside and a plug in the medulla. This uniting tissue is called the **provisional callus.** In animals it is generally converted into cartilage, but in man direct ossification usually begins in the third week. In man, however, when tolerable rest cannot be maintained, as in

fractured ribs and many fractures in children, cartilage may be developed. On the other hand, where the most perfect rest is obtained, as in fissures of the skull, little or no provisional callus is formed; it is always in greater quantity where the bone is thickly covered by soft parts, and rarely forms a complete ring in man. It is strongly developed in any angle or gap.

Ossification of the provisional callus begins in the angle between the periosteum and the bone, and extends thence beneath the periosteum and along the surface of the bone. The plug in the medulla ossifies a little later. At first the bone is soft and open in structure, and easily picked off the shaft. Its canals are more or less vertical to the surface of the shaft, and continuous with abnormally wide Haversian spaces in the latter. Ossification begins round the vessels passing from the callus to the bone, the cells most distant from each assuming the shape of osteo-blasts, and becoming surrounded by or converted into bone. Osteoblasts inside each ring now lay down lamina of bone until Haversian systems are formed. The callus is now intimately united with the original bone, and holds the ends firmly together. The medullary canal is blocked by bone, and osseous buttresses fill up any angle. This complete ossification of the provisional callus is finished in man between the fourth and eighth weeks, according to the size of the bone.

So far the bony tissue has not been mentioned. The next step is to unite the two ends directly by what is termed **permanent** or **definitive callus**. This is said to begin to form when the provisional callus has fixed the ends of the bones; but preparation for this union begins much earlier. The ends of the bones are to be softened into a tissue which can bridge over the gap, blend the two fragments into one, and finally ossify. A rarefying ostitis begins probably immediately after the injury, and results in a round-celled growth, which slowly eats away the walls of and enlarges the Haversian canals. Naturally this is a much slower process than similar infiltration of

the soft parts. So long as the bones are moving on each other, the granulations would have little chance of blending across the gap; but so soon as the fragments are fixed this union occurs, and ossification, running on to sclerosis, follows. It is probably not complete before the fourth month.

The final process in the union of a simple fracture is the rounding off of all prominences, and the absorption of all unnecessary provisional callus. The completion of this may occupy years; but, ultimately, in an accurately set fracture, the medullary canal may be opened up and most of the thickening around the shaft removed. Generally the seat of fracture remains evident, but Billroth says that in some cases it cannot be recognised (10th edition, p. 244). The analogy between the repair of bone and the repair of ordinary connective tissue, as described under healing of wounds, scarcely needs pointing out; ossification of the scar-tissue is the main difference.

Union of compound fractures is effected by the ossification of granulation tissue, either directly or after its conversion into fibrous tissue. But suppuration, indicating more or less destruction of the new tissue, and often necrosis of soft and hard tissues, greatly delay the process. Even where compound fractures become simple from the first by union of the wound they are often much longer in healing.

A wound in a muscle as a rule gapes widely and heals by granulation. In some parts, as the tongue, retraction is prevented and union by first intention occurs readily. The protoplasm escapes through the opened sarcolemma, and leucocytes penetrate for some distance between the fibres. Ordinary scar-tissue develops from the granulation tissue and unites the ends of the muscle. New cells are now produced by the muscle-cells on each side of the scar, and they invade and may eventually replace the cicatricial tissue. Kraske says that new muscle-cells are

produced by multiplication of the nuclei of the old. Each nucleus becomes surrounded by a spindle-shaped mass of protoplasm and divides to form muscle-fibres. In some cases no regeneration is evident.

Regeneration occurs more frequently to repair losses from degeneration, such as that which occurs in acute febrile diseases, especially typhoid. The new cells are believed to spring from small elements lying between the original muscle-fibres, or by splitting of the old cells from end to end.

Involuntary muscle-cells multiply also by division.

NERVE-CELLS AND NERVES.

Nothing is known of a regenerative process among ganglion-cells, and many think that none occurs in adult life. An ordinary scar is all that is known to replace destroyed ganglionic-tissue.

When a nerve is cut across union takes place readily by scar-tissue if the ends are brought together; and, as a rule, function is restored in the course of time, even when a considerable piece (in some cases nearly two inches) has been excised.

After division myelin escapes up to the nearest nodes of Ranvier, and blood is extravasated between the fibres and in the sheath. Then leucocytes infiltrate the ends for a short distance, rendering them bulbous; the soft parts are similarly infiltrated, and a mass of granulation tissue soon unites the ends. Later this develops into ordinary scar-tissue.

Beyond the degeneration of a few fibrils, no other immediate change occurs in the central end. In the peripheral end changes may be noted after twenty-four hours; they lead to destruction of the nerve. The following account is taken from Ranvier ("Leçons," &c., 1878), as quoted in Quain's "Anatomy:"—In warm-blooded animals, after twenty-four hours, the nuclei in the primitive sheaths are found enlarged, and the sheath is

everywhere visible; then protoplasm accumulates round the nuclei, at the nodes and other points, replacing the medullary substance. On the third or fourth day these protoplasmic masses are so large as to interrupt completely the sheath of Schwann at many points. At the same time the nuclei are seen to have multiplied once or twice. A little later, and almost all myelin has disappeared, the axis-cylinders are broken into short segments which may finally go, and nothing remains of the peripheral end of the nerve but the primitive sheaths, full of clear granular protoplasm, in which nuclei are abnormally frequent. Some drops of myelin persist. A few fibres do not undergo degeneration. They are thought to have sprung from other undivided nerves lower down, and to be taking a recurrent course in the divided trunk. These fibres degenerate in the central end. These changes are said to begin in the muscle-plates in motor nerves; but they occur practically at the same time throughout the peripheral ends. They are generally complete in fourteen days.

No regenerative changes occur for four or five weeks. Then it is found that the axis-cylinders of the central end are dividing into two bundles (which again divide several times) or into several, and that these small new axis-cylinders are finding their way through the scar-tissue into and between the old primitive sheaths. Growth of the axis-cylinders always begins from a node next above or close to the section. A cross-section of the peripheral end at about the eighth week shows small medullated and non-medullated nerves, among the old primitive sheaths, full of protoplasm. The course of these new fibres is very irregular, especially through the scar, where they may even loop back. At first non-medullated, they acquire, later, sheaths of Schwann, with nodes of Ranvier, which are at first placed at short intervals, as in young nerves. In the scar, primitive sheaths even are at first wanting; but they ultimately form from the surrounding connective tissue.

Some months pass before function is restored, a shorter time being required in sensory than in motor nerves, and it is supposed that during this time the axis-cylinders are slowly finding their way along the nerve. The number of axis-cylinders produced in this process is much greater than that of the nerves destroyed. It seems probable, therefore, that many atrophy; but their further history is not known.

Cases occur in which restoration of sensation takes place within a few days of the division of a nerve. It has been supposed that "immediate" union of the ends took place, but this is unlikely. The explanation is probably that communicating nerves take on the function of the divided one.

EPITHELIUM.

Epithelium is always derived from pre-existing epithelium, by simple division of the cells. This is shown by the fact, that it always spreads in from the edge of an ulcer, unless islets of the rete have been left undestroyed in the midst of the granulation tissue.

The epithelium of the skin and mucous membranes, and probably also of all glands, is being destroyed and replaced throughout life—sometimes very rapidly, as in catarrhs of mucous membranes.

Epithelium is the tissue which better than any other bears transplanting. Use is made of this in the operation of grafting, in which small bits of the superficial part of the rete are placed upon a healthily granulating surface. They are nourished by the exudation at first, grow and adhere, forming centres, whence epithelium spreads over the surface. The cells of the root-sheath of hairs answer the purpose well. Granulation tissue may be skinned over in this way; but unless it forms scar-tissue, the cicatrix breaks down readily. Ordinarily, contraction precedes the skinning over.

Regeneration of nails and hair is frequent.

CHAPTER XLV.

SEPTICÆMIA AND PYÆMIA.

THE diseases known as Septicæmia and Pyæmia result from the absorption and dissemination of substances derived usually from the septic discharge of some wound or acute inflammation. The two diseases are frequently associated.

By "Septicæmia" is now generally understood those forms of septic disease which are unaccompanied by the development of secondary inflammations. "Pyæmia," on the other hand, no longer means disease due to the absorption of pus into the blood, but includes cases of septic disease characterised by the presence of secondary or metastatic suppurations. These two maladies are the chief elements in the excessive mortality in large general hospitals, and nothing is more clearly established than that overcrowding of patients with septic wounds is indirectly their chief cause. By this process the diseases may speedily be generated anywhere. In almost all cases of both diseases there exists a wound to which unpurified air has gained access, or which may have been inoculated directly from a similar case.

The pathology of these diseases has been worked at by many observers, but the results obtained were too uncertain and too often contradictory to be of much value until the appearance of R. Koch's small book on Traumatic Infective Diseases (translated by Cheyne, New Sydenham Society) in 1878. In this work Koch made known methods of research which were vastly more certain than any which preceded them, and which have since been improved upon. His account of the results which were attained by these methods, and the admirable Report on the Nature and Causes of Pyæmia, Septicæmia,

and Purulent Infection, presented to the Pathological Society in 1879 by a special Committee,* will be freely utilised in the present chapter.

SEPTICÆMIA.

Koch injected five minims of blood or meat-infusion, in an early stage of putrefaction, under the skin of a house-mouse; the animal at once became restless and ceased eating; its movements soon became weak and uncertain, respiration irregular and slow, and death occurred in 4—8 hours, or even earlier, the time of its occurrence varying with the size of the dose. No pathological change was found in the body, and blood inoculated on healthy animals produced no effect. The disease was not infective. We have here a disease due to the absorption into the blood of putrid material, not characterised by secondary inflammation; it is therefore a septicæmia. It seems to be due to the presence of a chemical poison in greater or less quantity in the blood, and is comparable to the result of the injection of a poisonous alkaloid. This would exercise its specific action upon the organism, and would, of course, not multiply in the body; the original dose being diluted by the blood-mass, a few drops of the latter injected into a healthy animal would have no effect. This form of septicæmia is called **Septic Intoxication.** From an extensive series of experiments Sanderson gives the following as its symptoms:—Restlessness, muscular twitching, and increasing weakness till the animal falls; vomiting and profuse diarrhœa, the fæces being at first loose, whitish grey, but later bloody; the temperature rises some degrees at first, often falling below normal before death; respiration and heart-action gradually fail, and death is sometimes preceded by cramps. The corresponding post-mortem appearances are:—blood dark, feebly clotted; petechiæ beneath peri- and endo-

* Trans. Path. Soc. Lond., 1879.

cardium and pleura; intense staining of the endocardium and lining membranes of the great vessels, and often a little blood-tinged serum in the serous cavities, both soon after death, indicating destruction of red corpuscles even during life; intense congestion and ecchymosis with shedding of the epithelium of the mucous membrane of the stomach and intestines; spleen swollen, soft, and pulpy; liver often swollen and congested.

As would be expected, when less poison is introduced, the resulting symptoms are less marked, and are quite absent when one, or at most two, drops of putrid blood have been injected. After the use of such small quantities of blood mice often remained permanently well. But about a third of them sickened after about twenty-four hours, the symptoms being characteristic and constant, and not preceded by the above toxic effects. They were as follows:—Dulness of the eye with increased conjunctival secretion, finally glueing the lids together; the animal moved little and languidly, and generally sat still in peculiar attitude; it ceased to eat, its respirations became slower, weakness steadily increased, and death came on almost imperceptibly forty to sixty hours after inoculation. Post-mortem there were found:—slight œdema, which is often absent, at the site of injection or inoculation, and considerable swelling of the spleen, other organs appearing normal.

It is sufficient in order to cause death in about fifty hours, and with similar symptoms, to touch with a knife at the point most remote from the seat of inoculation the subcutaneous tissue of a mouse dead of the disease, and with this knife to scratch the ear of a healthy animal.

Here again we have a disease which must, according to our definition, be called Septicæmia. But it differs from that form first described, in being intensely *infective*. Only a minute quantity of poison is introduced—quite insufficient to produce toxic effects—and it multiplies enormously in the blood. Some twenty-four hours of incubation pass whilst its development reaches a certain

stage, with its further increase the symptoms become more severe. This form is known as **Septic Infection**.

The blood of animals which died after *injection* of 1-10 m of putrid blood, generally contained varying numbers of cocci, bacteria and bacilli; but after *inoculation* it contained only small bacilli. These were present in large numbers, most white corpuscles containing one or many of them. Koch thinks they grow into the vessels about the seat of inoculation, and become generalised in this way; he has never seen them in lymphatics. They occur in all parts, and are not more numerous in the swollen spleen than elsewhere.

Koch failed to infect either rabbits or field-mice with this disease. The latter result seems very curious; but Koch points out that there are obvious differences between the blood of the two animals, so it is easy to imagine that differences may exist which render the blood of the one suitable, that of the other unsuitable, for the development of these particular fungi.

Under the heading Septicæmia, we have therefore two diseases—**septic intoxication,** non-infective, due to the absorption of a chemical poison manufactured in some putrefactive process external to the body; and **septic infection**, due to the entry of specific fungi into the blood, and to their multiplication there. The organisms probably act by producing poisonous substances in their growth, but these products are not irritant, and therefore no secondary inflammations arise. The fungi which characterise the septicæmia of one animal differ from those which occur in that of another—*e.g.* bacilli in mice, oval cocci in rabbits. Every putrid fluid probably does not contain the organisms of each of these diseases. The production of septic infection from putrid fluids is therefore uncertain. Thus Koch notes that on two separate occasions he succeeded with putrid meat infusion in producing in rabbits the same disease, characterised by the same cocci.

In Man the occurrence of analogous forms is *a priori*

likely, and cases might be quoted in which the existence of pure septic intoxication or septic infection was very probable; but the subject has not been at all fully worked out. Clinically, it is often impossible to diagnose between them, and the post-mortem signs are very similar. The symptoms of septicæmia in man are fever, often beginning with a rigor, which may be repeated, especially in the infective form; all the symptoms of fever, including delirium, sometimes violent, passing on to stupor or even coma. There are great loss of strength, rapid emaciation, dry tongue, and rapid, feeble pulse—the "typhoid" state appears early. Vomiting is common, diarrhœa much less so; but cases do occur in which the symptoms and pathological changes of gastro-enteritis are well marked. A jaundiced tint of skin is not uncommon, and petechial spots may occur. Albuminuria is frequent. In the infective form death occurs quietly in a semi-comatose state, and after a longer period than the non-infective, the characteristic ending of which is speedy collapse—the patient dying with some dyspnœa, and all the symptoms of rapid cardiac failure.

The red corpuscles in blood drawn during life run into clumps instead of rouleaux; and Huter states, as the result of observations on the palpebra-tertia of infected animals and on the lip of man, that in septicæmia there is wide-spread capillary stasis, perhaps, half the capillaries in a district being full of resting blood in severe cases. Frequently, too, small clumps of red corpuscles pass across the field or stick in some vessel.

The post-mortem signs are:—Feeble rigor mortis and early decomposition; the blood may be dark and fluid, but is more often clotted as usual; there is deep staining soon after death of the endocardium and lining membrane of the great vessels, and any serous fluid in the pleuræ or pericardium will be blood-tinged—this is owing to rapid disintegration of red corpuscles, which begins even during life; petechiæ occur beneath serous membranes, chiefly on the back of the heart and under the pleura; hypostatic congestion of the lungs and congestion of the

abdominal viscera would be expected under the circumstances; the spleen is markedly swollen and often pulpy; and, lastly, the mucous membrane of the alimentary canal may be congested, or much more rarely inflamed.

Organisms, especially cocci, have often been found in various parts and organs in septicæmia; they have also often been missed. Even when found, no characteristic form has been shown to be present.

Marcus Beck calculates from the results of experiments on dogs, that 1–2 oz. of putrid serum or pus would be required to kill an adult man by septic intoxication. This form can, therefore, occur only where *large cavities* exist and *are imperfectly drained*—*e.g.*, in bad compound fractures, wounds of joints, or pleuræ, abdominal sections, the uterus post-partum, &c. Such cavities cannot always be drained; hence the necessity for also preventing putrefaction. Raw surfaces and serous membranes are well known to be excellent absorbing surfaces. A large quantity of poison may be taken up by them in a short time. Granulating surfaces on the other hand have been shown by Billroth not to absorb the putrid poison. Hence **septic intoxication** will be most likely to occur *before granulation begins*. It may occur later if the granulation-tissue is destroyed in any way.

Septic Infection may occur from the smallest wound, and there may be distinct evidence of inoculation of a poison. The presence of only a *small wound* of evidence of inoculation of a septic poison, and the discovery of organisms in the blood during life would show that a case of septic disease was infective.

Fever from three causes, apparently, may follow on an injury. If this is subcutaneous or preserved from decomposition the fever is called **aseptic traumatic fever.** This is said to be due to absorption of the exudation which results from the injury, and which contains a quantity of *fibrin-ferment.* This body has been shown by Köhler to be pyrogenous. It is usual for the temperature to rise to 100° F. or so after simple fractures and severe contusions. Next,

inflammation may occur at the seat of injury from tension and like causes, without any decomposition or infection of the wound; quantities of exudation are absorbed, and fever in proportion excited. This is **simple inflammatory fever**. Lastly, the discharges from a wound may putrefy, and the chemical products of putrefaction are absorbed, giving rise to what has ordinarily been called *traumatic* or *surgical fever*. It is best spoken of as **septic traumatic fever**. It sets in with commencing putrefaction on the second day, reaches its maximum on the third or fourth, and then falls *as the wound granulates*. It varies much in severity, the temperature being commonly 102°–104° F.; and no line can be drawn between it and *septic intoxication*, the amount of poison absorbed constituting, apparently, the only difference. Its occurrence does not prevent the causes of aseptic fever also from acting.

With regard to the cause of septic intoxication—many of the products of putrefaction are pyrogenous. Bergmann succeeded in crystallizing in fine needles from putrid fluids an alkaloidal body which he calls sepsica, which possesses in a high degree the property of exciting fever.

Pyæmia differs from septicæmia in this respect, that in it the absorption and dissemination of the poison gives rise not only to a general disease, but also causes the formation of secondary foci of inflammation—so-called **metastatic abscesses**. These are the distinctive pathological characteristics of the disease. Its clinical symptoms are well marked, the very irregular temperature being most important; but it is confessedly complicated with more or less septic poisoning.

Like septic infection, the disease is essentially a hospital-disease, and their poisons are probably similar; some indeed believe them to be the same. The source of infection is almost always some wound or inflammation, generally

suppurating, the discharges not being aseptic. But there may be no wound, as is seen in acute infective periostitis, infective endocarditis, and rare cases of "spontaneous" pyæmia in which no primary lesion can be found. In these cases the poison has probably entered through some healthy mucous membrane. As in septicæmia, it gains access to, and is distributed by, the blood.

Besides the secondary abscesses, the following signs may be found post-mortem. As in all septic disease, rigor mortis is feeble and decomposition early. Emaciation is generally marked, and the skin yellow or jaundiced. Petechiæ may be present. The wound, if there is one, is sloughy, perhaps surrounded by diffuse inflammation, and offensive; any bone which has been divided shows the appearances of septic osteomyelitis. The thrombi in the veins leading from the focus of infection are extensive, and undergoing infective puriform softening; the end of one or more thrombi perhaps projects into a large vein in which circulation was going on. The blood is generally normal to the naked eye, but microscopically contains excess of leucocytes. Hypostatic congestion of the lungs is generally present, the spleen large and pulpy, and the liver and kidneys show "granular degeneration."

The secondary abscesses are of two kinds—those which follow upon infarction, and those in which there is no evidence of such an antecedent change. In either case, the occurrence of suppuration implies the presence of a strong irritant acting for some time, and it has been already pointed out (p. 291) that most irritants of this kind are fungi. It is probable that several fungi are capable of exciting suppuration, and they would therefore, if generalised by the blood-stream, produce the abscesses of pyæmia. It seems possible, therefore, that for example the organism which produces acute necrosis may not be the same as that of ordinary pyæmia from wounds.

However this may be, in the first kind of abscess, infarction is induced by the lodgment in a terminal artery

of a portion of infective clot. The mode of formation and characters of the infarct and abscess has been described on pp. 214 and 243. The preparation for embolism has been noted above in the account of the veins leading from the focus of infection. These embolic abscesses are by far most frequent in the lungs, next in the liver, spleen, kidneys, and brain. They may occur in any vascular part. They lie generally upon the surface of organs, with their bases immediately beneath the capsule. They vary in size between that of a chestnut and that of a split pea, are usually multiple, and may be very numerous. They are surrounded by the usual hyperæmic ring. Often more than one organ is affected, and these abscesses may occur with others of the next kind. Sometimes the lungs are not affected, when other organs lying beyond them on the blood-path are.

The second kind of abscesses are diffuse suppurations in the subcutaneous and intermuscular connective tissue, in the joints and serous membranes. They are all tolerably common, and may occur alone or combined with the first variety. In these cases the irritant must be conveyed to the spot by the blood and settle there, probably because the nidus is suitable, or perhaps some capillary embolisms are the cause.

Pyæmia has never been produced in animals by the injection of blood or pus of pyæmic patients. Cocci and zoogloea masses are found in abundance on the surfaces of the focus of infection, the intensity of the process varying with their number, according to Birch-Hirschfeld. They have been traced into the surrounding tissues, and been seen piercing the wall of a vein. They have been found in the nearest lymph-glands, in all metastatic abscesses, and in many organs. They lie in capillaries or small arteries primarily, but soon pass out into the surrounding tissues.

Koch injected 10 ℳ of putrid fluid, in which a portion of skin had macerated, into a rabbit. No symptoms followed for two days; then the animal ate less, became weaker, and

died 105 hours after the injection. A purulent infiltration occupying the abdominal wall far around the point of injection was found; the inflammation had extended to the peritoneum, and there was general fibrinous peritonitis. The spleen was much enlarged, the liver had a greyish mottled appearance, and showed on section grey, wedge-shaped patches. In the lungs were some dark-red patches about as large as a pea, and airless. Animals inoculated with the blood of this one died of precisely the same disease. The smaller the dose the longer the time before death. This is explicable only on the supposition that the infective particles in the blood must reach a certain number in proportion to the body-weight before they can cause death. Micrococci were found everywhere, especially in obviously altered parts. They adhered to the interior of vessels, often plugging them. Red corpuscles adhered to the coccus colonies which seem able to induce coagulation; small thrombi are thus formed, which may be swept away as emboli, and would prove infective. Perhaps something of this kind may account for the second kind of abscess. The resemblance of the whole disease to pyæmia is very marked. It is not certain, however, that pyæmia in man is always infective.

CHAPTER XLVI.

THE VEGETABLE PARASITES.

By STANLEY BOYD, M.B., F.R.C.S.

Parallel between Fermentation and Infective Disease.—It has long been thought that the group of acute specific diseases must have a very special cause. The characteristics of this group are:—That they occur epidemically; that they are obviously contagious and infectious; that each member is absolutely distinct from its fellows,

and runs a very typical course; and that the poison which gives rise to each of them multiplies in a marvellous manner—a single case of one of these introduced into a community may cause the death even of millions. Nothing could be discovered by the senses to account for the appearance of these diseases; yet they were obviously produced by something which multiplied in the sick, which clung about his clothing, &c., perhaps for long periods, and which could be carried through the air for considerable distances. This "something" is called the "**contagion**" of the disease; and for many years science has been endeavouring to discover its nature. It early became obvious that no gas would meet the requirements of the case, for diffusion would soon put an end to its power for mischief; a fluid was not to be thought of; so contagion was necessarily regarded as a solid in a state of very fine division—*particulate*. It has been shown to be insoluble in fluids in which it can live by subsidence (vaccine, Chauveau), and by filtration, the poison not passing through the filter. These facts, taken with its power of multiplication, seemed to show that the contagium was some living organism; hence the origin of the **contagium vivum** or **germ**-theory of disease. So early as 1840, Henle expressed the belief that living organisms, probably of a vegetable nature, were the causes of the acute specifics. Two years earlier Bassi and Audouin had discovered the fungous nature of the muscardine disease in silkworms; and in 1836, Schwann and Cagniard de Latour had independently discovered that yeast, the apparent cause of alcoholic fermentation, consisted of cells, multiplying by budding, and apparently of vegetable nature. They surmised that the decomposition of the sugar into alcohol, carbonic acid, &c., was connected with the growth of this plant.

Long before this it had been noticed that a close parallel might be drawn between an infective disease and a fermentation. It may be presented thus:—

Infection	Addition of ferment.
Incubation	Period during which nothing is noticed.
Fever, outbreak, and course of disease . . .	Rise of temperature, and active fermentation.
Decline of disease . . .	Gradual cessation.
Period of protection from same disease	Addition of more ferment has no effect.

It may be further noted that, except in cases in which yeast was added to the saccharine liquid, the source of the ferment in cases of alcoholic fermentation was as mysterious as was the source of the poison which gave rise to an epidemic of whooping cough.

Etiology of Fermentation.—The above parallel was generally recognised; and the cause of fermentation being much more open to experiment than the cause of infectious disease, was taken up by many workers. Many kinds of fermentation were speedily recognised—lactic, butyric, viscous, &c.; and the close relation of putrefaction to these processes was soon acknowledged. In each one of these organisms were found, and their relation to the processes has been the moot point between the upholders of the vital or germ theory of fermentation, and the supporters of the physical theory. The alcoholic fermentation has been used as the type of all.

The Germ Theory, started by Astier, Schwann, and Cagniard de Latour, and perfected by Pasteur, is adopted by the great majority of scientific men at the present day. According to this view, the Saccharomyces cerevisiæ (yeast plant) is the *cause* of the alcoholic fermentation. Its food is sugar, together with nitrogen and some inorganic materials, which must also be provided; the products of its life-action are alcohol, carbonic acid, glycerine, and succinic acid. It is supposed that the food-stuffs pass into the cells, which take what they require for their own growth and repair, and throw back into the fluid the products of their action. Thus a yeast-cell forms the above-mentioned substances just as a hepatic cell forms

the constituents of bile. There is no reason whatever for classing the fermentations as distinct from the chemical changes effected by cells in general. The division was made before their nature was understood, when the insignificance of the cause and the greatness of the result were the striking features, and when the causal relationship between the growth of living organisms (or the presence of a substance derived from them – *unformed* ferment) and the chemical changes had not been proved.

The Physical Theory, started by Willis in 1659, and perfected by Liebig, affirms that fermentation is a "molecular motion" transmitted to unstable organic compounds (fermentable substance) by albuminoid particles (ferment) which are themselves the seat of "motor decay" (*i.e.*, are undergoing decomposition). The molecular motion of these particles may initiate in a large amount of a more stable substance changes similar to those of which they are themselves the seat. Any portion of the substance to which this molecular motion has been communicated is capable of transmitting it to other suitable material, and thus the ferment *seems* to multiply. The ferment communicates its vibrations to the particles with which it comes into contact, and these again to particles next beyond, more slowly but in the same way as a spark causes the decomposition of a train of gunpowder. Bastian says that there is no proof of multiplication other than occurs in a sufficiently strong solution of sulphate of sodium when a crystal of the same salt is thrown in. Gerhardt thus illustrates Liebig's views:—Every substance which decomposes or enters into combination is in a state of movement (molecular). Various forms of mechanical agitation provoke this movement (*e.g.*, decomposition of chlorous acid, chloride of nitrogen, fulminating silver); therefore chemical decomposition, in which the agitation is more complete, should produce such effects more strongly. It is known that platinum remains stable in nitric acid, but if silver also (which dissolves in nitric

acid) is present the platinum is dissolved; again, pure copper is not dissolved by sulphuric acid unless zinc is present. A solution of dextrine is not acted on by yeast alone, but when sugar is added to the fluid a great part of the dextrine shares the fate of the sugar, the motion of the atoms of sugar having been transmitted to those of the dextrine. By analogy Liebig supposes that sugar does not change when quite alone, but decomposes—*i.e.*, ferments, when in contact with a nitrogenous body (ferment) undergoing change. This view originated long before the constant presence of specific forms of organisms in every fermenting substance was demonstrated. Before Liebig died, however, Pasteur had gone a great way towards this; and in his last paper* on the subject Liebig—though still fighting against the germ theory—states that it is not opposed to the molecular motion theory which he advocated; the decomposition would still be due to molecular motion transmitted to the fermenting substance by living protoplasm instead of decaying albuminoid material. As nothing is known of the force by which living cells effect chemical changes, it is impossible to confirm or to deny this statement.—(Quoted from "Beginnings of Life," Bastian.)

It is very difficult absolutely to disprove the physical theory. Its supporters admit the frequent presence of organisms in fermenting fluids, but regard them as accidents, or as spontaneously generated (Bastian), for the same decompositions can be effected in their absence. Thus dilute alcohol, run over wood-shavings or charcoal so as to expose a large surface to air is converted into vinegar. But this is no evidence against the ability of the Mycoderma aceti also to effect the oxidation as a vital act; and indeed distinct differences exist between the two processes (Schützenberger, page 237).

The difference in form and mode of growth of the organisms characteristic of the different fermentations is

* Ann. d. Chemie u. Pharm., vol. cliii. p. 1, 1870.

accounted for by supposing that the conditions in each favour the growth of a certain organism, or the origin *de novo* of a certain fungus (Bastian). The organisms formed in any fluid may be cultivated again and again in artificial fluids and thoroughly washed with distilled water; the reaction characteristic of the fermentation whence it was taken will still occur if the organism be now inoculated upon a suitable fluid. It would seem then, upon the physical theory, that the "particles in a state of motor decay" adhere very closely to the organism which is constantly present, and are able to impart their molecular motion to such substances only as this organism will grow in. For if the organism dies no fermentation occurs.

The particles in a state of motor decay have never been demonstrated in such a manner as to avoid the suspicion that organisms were also present. So-called "antiseptics," which are selected on account of their ability to destroy the lower organisms, invariably check the molecular motions of the physical ferments; so also does heat sufficient to destroy organisms. In fact, the properties of the physical ferments are those of organisms.

Finally, it has been shown of several fermentations that the thinnest membrane, the shortest column of fluid, is sufficient to prevent the transmission of these supposed vibrations; that direct contact with the ferment is necessary; and that sonorous vibrations have no influence upon fermentable substances (Dumas). If a solution of sugar in a test-tube is divided into two parts by a plug of cotton-wool and yeast is introduced into the upper, this only ferments, though fluid continuity in uninterrupted.*

We must therefore conclude that although the physical theory may be theoretically possible, the evidence goes to show that the vital theory is practically true; and that *all the processes generally known as fermentations and putrefaction are due to the action of vegetable organisms.*

* Hoffmann, Ann. d. Chem. u. Pharm., cxv. p. 228.

How do these organisms act? The four following views are held :—

(1) Like all living cells they require certain materials for the repair of their substance and for growth. They take into their substance the organic and inorganic compounds which are necessarily present in any liquid in which they will grow, and they throw back into the fluid the products of their action upon these compounds.

(2.) Pasteur has stated that fermentation in general is a consequence of the life of ferments without oxygen. They require oxygen so much, that they take it from the organic substances, and thus split them up. But, holding this view, it is not clear how Pasteur can at the same time say that oxygen is harmful to the butyric ferment.

(3.) Certain, and perhaps all of them produce *unformed* ferments—so called in opposition to the cells themselves, which are the "formed" or "organised" ferments. The chief characteristics of these bodies are :—that they seem to act by mere contact ("catalytically"), not taking any part in the decompositions to which they give rise; that they act in extremely small quantity; do not multiply, but, nevertheless, transform many times their weight of the fermentable substance ; that they are soluble, and are always derived from living cells; that, like cells, they act best at a certain temperature, their action being arrested at a low or high temperature. They have not been isolated in sufficient quantity for accurate analysis. Ptyalin, pepsin, trypsin are well-known examples from the human body; emulsin (bitter almond) and diastase (barley) from the vegetable kingdom. It is certain that some bacteria (*e.g.*, putrefactive) form amylolytic and peptic ferments, which can be separated from, and will act in the absence of, the organisms. Musculus has separated from Micrococcus ureæ a body capable of changing urea into ammonic carbonate. Yeast, by an unformed ferment, transforms cane-sugar into glucose and lævulose, before converting it into alcohol, &c.; but this latter change has never been effected in the absence of living

cells. Whether acting upon hydrocarbons or albuminoids, it is believed that these ferments generally cause simple taking up of water and splitting of the compound. It has been suggested that their action is that of a carrier, like haemoglobin, or like the sulphuric acid in the manufacture of ether from alcohol.

4. Nageli has adopted Liebig's view to a certain extent—the life and growth of cells is necessary to fermentation, the chemical changes being always due to the transmission of the molecular motions of *living* protoplasm to the unstable compounds around it.

Products of Fermentation.—It is impossible to say much in a general way of the products of fermentative processes, for they are as various as are the processes themselves and the organisms which are believed to give rise to them. They are formed by processes of oxidation and deoxidation, of hydration, and of simple splitting up. The same food will, under the action of different organisms, be converted into very different substances. Thus, sugar undergoes vinous, lactic and butyric, mucous and mannitic fermentations. Other products than those from which the process takes its name are always formed. Gases are sometimes evolved, sometimes *not*. In many processes bodies are formed which hinder the development of the organisms which produce them; thus, the alcoholic fermentation is checked by accumulation of alcohol, and putrefaction by the development of bodies like carbolic acid and cressol.

If the analogy, pointed out on p. 475, between infective diseases and fermentation were certainly true, we might at once infer that the former are caused by the growth and life-action of vegetable organisms in the tissues of the body. But no one could accept the conclusion on the evidence of so superficial a resemblance. The same stringent proofs must be afforded in the case of each disease as were demanded in the case of each fermentation. How far these

proofs are forthcoming will be shown in the concluding part of the present chapter. Many low forms of vegetable life have been found in connection with diseases in man; and we shall now state what is known of their botanical position and life-history.

NATURAL HISTORY OF THE VEGETABLE PARASITES.

The vegetable organisms, which have been found connected with the diseases of man, are all **Thallophytes**, or plants in which no distinction between stem and leaf exists; and, as they are all destitute of chlorophyll, they belong to the class of **Fungi**—*not* Algæ. The pathological fungi are of three kinds—**Bacteria** or **Schizo-mycetes**, **Yeasts** or **Blasto-mycetes**, and **Moulds** or **Hypho-mycetes**. The bacteria, besides causing putrefaction and several of the "fermentations," include almost all the organisms which are believed to produce the infective diseases. They are, therefore, by far the most important group.

The **Schizo-mycetes** are a-chlorophyllous, uni-cellular organisms, many of which approach the limits of microscopic visibility, whilst all are very small. They refract light strongly, and cause turbidity of any culture-fluid in which they may be. They consist of a peculiar form of protoplasm, *mycoprotein* (v. Nencki), and appear structureless; but it is very probable, from their great resistance to alkalies and dilute acids, that they possess a cell-membrane of a substance allied to cellulose. In form they vary much, being round, oval, dumb-bell-shaped, rod-shaped—straight, wavy, or corkscrew-like. They are never branched. They multiply by transverse division, which occurs in the rod-forms at right angles only to the long axis, but which, in the round, may take place in two directions at right angles to each other (Sarcina). In a certain number of bacilli spore-formation, alternating with fission, has been observed, sometimes preceded by growth of the rods into long filaments (*leptothrix*), sometimes not. The new cells formed by fission may at once

separate from the parent; or they may remain united to each other end to end, forming chains, or lying side by side in more or less spherical colonies, bound together by a viscid intercellular substance—**zoogloea**—formed of swollen cell-membrane (Cohn) or of mycoprotein (v. Nencki). The time occupied in division has been variously given at from ten to thirty minutes; and, as the offspring proceed at once to divide like their parents, a single bacterium may, in twenty-four hours, give rise to a progeny which Cohn estimates at over 16,000,000.

Single round cells have no movement other than Brownian; but chains and colonies of them do seem capable of locomotion (Ogston). The rod-forms have often a mobile and a motionless stage; but some never move—*e.g.*, B. anthracis. In some cases one or two cilia have been found; in others the mode in which motion is produced is unknown. Often no reason can be assigned for a change from motion to rest, or *vice versâ*. A good supply of oxygen seems to be connected with active motion of some forms.

CONDITIONS OF LIFE.—Food.—Each variety of fungus seems to differ more or less from all others in its food-requirements; but all must be supplied with the materials from which they can obtain the elements of which they consist. These are carbon, hydrogen, nitrogen, phosphorus, sulphur, calcium, magnesium, and potassium. The first four are generally provided by carbohydrates and albuminoids; the rest by inorganic salts present in animal and vegetable tissues. Certain bacteria, however, can assimilate nitrogen and carbon from much less complex compounds than albumen and carbohydrates, as is shown by the growth of putrefactive organisms in Cohn's fluid (phosphate of potash, ·5; sulphate of magnesia, 1; phosphate of lime, ·05; tartrate of ammonia, 1; water, 100); to others, the more complex bodies are essential. Thus beer-yeast will not grow unless glucose or some body convertible into it is present; the Bacillus tuberculosis grows best in blood-serum. It is probable that a fluid

could be discovered for each fungus and placed under such conditions that it alone would grow in it. Raulin has worked out the composition of such a fluid for a mould (Aspergillus niger), and has proved the value of each constituent, no matter how small in quantity, by a diminution in weight of the dried plant yielded by a certain quantity of the fluid.* Whereas, in Nature, it is frequently stifled by other organisms more suited than itself to the existing conditions, it here gets the upper hand of all. Very slight differences in the composition of the food-material may favour the growth of one organism rather than another. Nageli says that in a neutral fluid containing sugar, in which were moulds, yeasts, and bacteria, only the latter flourished —causing lactic fermentation; the addition of half per cent. tartaric acid brought the yeasts to the fore, with production of alcohol; and the addition of 4–5 per cent. tartaric acid caused the moulds to develop. The reaction of the fluid has a marked influence in this respect; as a rule acidity is unfavourable to the development of fungi, alkalinity favourable. As showing what a very slight difference may suffice to prevent the growth of a bacterium, it will be remembered that Koch was unable to inoculate a field-mouse with an organism which always produced fatal septicæmia in a house-mouse (p. 468). Some similar difference would seem to exist between two men exposed to the poison of an acute specific, one of whom catches it, whilst the other does not. We must therefore bear in mind that a very slight, to us imperceptible, change in the metabolism of the body or of a part, may enable organisms to flourish there, though previously unable to do so.

Water.—The presence of some water is essential to the development of all fungi—the moulds requiring less than the yeasts and bacteria. It is easy to add too much or too little for a given species.

Oxygen.—Pasteur has divided fungi into **aërobious** and

* Duclaux, "Ferments et Maladies," p. 43.

an-aërobious, according as they require or do not require free oxygen as a life-condition. Certain fungi, as Aspergillus niger, B. anthracis, die in the absence of free oxygen. Others are able to live both with and without it—at least for a considerable time—as Mucor racemosus (a mould), ordinary yeast, and Bacterium termo. Finally, the life-history of a few seems to be completely anaërobious; to Clostridium butyricum (butyric acid ferment) and Bacillus septicæmiæ of rabbits, air is said by Pasteur to be not only unnecessary, but even fatal.

Temperature.—Each organism flourishes best at a particular temperature. All will grow less actively at temperatures above and below this point; but the range within which growth will take place may be very limited, as in B. tuberculosis. The general statement may be made, with regard to Bacteria, that reproduction ceases in all these organisms at 5° C., and in many at a much higher point; but they do not necessarily die. Though rendered rigid and motionless (*rigor frigoris*), some are said not to be killed by the greatest cold; the spore-bearing B. anthracis has been exposed to −140° C. without injury. By rise of temperature, *rigor caloris* and death are induced; more easily in moist than in dry conditions, and much more easily in the adult than in the spore-form. Cocci and bacteria appear to be first affected by rise of temperature, then bacilli, and finally spores. Boiling, and indeed a much lower temperature than 100° C., will kill many fungi; boiling, continued for one to two hours, will certainly destroy all non-spore-bearing organisms; but solutions containing spores will not be sterilised by 100° C. unless it is continued many hours. Thus Tyndall failed to sterilise a hay-infusion by eight hours' boiling. This prolonged resistance of spore-containing fluids to boiling is explained by supposing that fresh generations of adult organisms are developed after the boiling is over from spores able to resist 100° C. for a long time—a view supported by the fact that such fluids are sterilised by boiling for a few minutes only

at intervals of several hours or a day. For certain sterilisation, solutions should be raised to 115° C., in a chloride of calcium bath for at least half an hour.

It is found that *dry* spores of B. anthracis are not destroyed by less than three hours' exposure to 140° C. Simple drying kills some bacteria, as B. anthracis, the spores of which may be kept in a dry state for years.

Rest.—Fungi flourish better in a still medium than in one of which the particles are moving constantly; whilst B. anthracis divides actively in the blood-stream, other kinds (micrococcus septicus) seem always to settle before multiplying.

These are the essentials to the **growth** of the plants which we are considering; but absence of growth does not necessarily mean death of the organism. If the conditions are unfavourable the cells will not develop; but they may not die. By making a sufficient change in any one of the above conditions, the development, and consequently the action, of any given organism may be prevented. Use is constantly made of this fact to preserve substances which would otherwise ferment, and to destroy germs which have already gained entrance to them.

ANTISEPTICS AND MODES OF DISINFECTING, &c.—Supposing that a suitable nidus for the development of fungi is provided, their growth may be prevented by adding to the fluid in sufficient quantity any one of a long series of bodies known collectively as "antiseptics," because being strongly antagonistic to cell-life, they prevent the development and consequent action of putrefactive bacteria; in other words, they keep things "sweet." The group includes vegetable and mineral astringents, resins, essential oils, many products of tar, chloroform, chloride of sodium, boracic, and salicylic acids, &c. &c. They vary greatly in power, however, and because one of them is very deadly to a certain organism it by no means follows that it will be so to another. It is always found that a smaller percentage of an antiseptic will prevent the development of organisms than will check their development once it

has commenced. The strength of the most dilute solution of an antiseptic which will prevent putrefaction is spoken of as its "efficient strength." It is very important to know this, for all antiseptics irritate and destroy animal, as well as vegetable, cells, and most of them are actively poisonous. The problem, therefore, is to discover for use in medicine those bodies whose action is certainly fatal to the parasites it is desired to kill, and which, at the same time, do the least possible injury to the human organism. The efficient strength of an antiseptic is found by adding it to putrescible fluids, and noting the quantity that must be present to prevent putrefaction. For special organisms, such as *B. anthracis*, special observations must be made upon fluids containing them. Buchholtz* gives the following as the efficient strength of the most commonly employed antiseptics:—

Mercuric Chloride	$\frac{1}{220\,000}$	Salicylate of Soda	$\frac{1}{850}$
Thymol	$\frac{1}{2500}$	Carbolic Acid	$\frac{1}{850}$
Benzoate of Soda	$\frac{1}{2000}$	Quinine	$\frac{1}{800}$
Creasote	$\frac{1}{1000}$	Cupric Sulphate	$\frac{1}{175}$
Benzoic Acid	$\frac{1}{1000}$	Boracic Acid	$\frac{1}{135}$
Salicylic Acid	$\frac{1}{850}$	Zinc Sulphate	$\frac{1}{85}$
Eucalyptol	$\frac{1}{850}$	Alcohol	$\frac{1}{85}$

The best antiseptics for use in the form of gases, are iodine and chlorine; sulphurous acid is very uncertain. All are most active in watery solutions.

Reference may here be made to Raulin's and Nägeli's experiments, given at p. 484, as showing that among fungi, as elsewhere in the living world, the struggle for existence is going on. Two kinds do not grow equally well in the same liquid; one is better adapted, or possesses greater power of adaptation, to the surrounding conditions than the other, and will, slowly perhaps, but surely outlive it.

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* Antiseptica u. Bakterien. Arch. f. Exp. Path., vol. iv. p. 1, 1875.

at interval ation of one or other species may be greatly
isation, s by experimental variation of the conditions so
of calcivour markedly one or the other organism. This
It ,onism exists not only between fungus and fungus,
de: probably also between invading fungi and the cells
of the animal body—suggesting an explanation of the way in which the cloud of healthy leucocytes at the margin of a spreading infective inflammation ultimately checks its advance.

Removal of Water.—Drying is a common method of preserving things. Healing under a scab and the dressings (cotton wool, &c.) which imitate this are examples of its use in surgery. Drying kills some fungi, but it only checks the development of others, especially spores. Sugar is not an antiseptic, but acts by abstracting water when it is used in the treatment of wounds, in the preservation of fruit, &c. If enough is not added to jam, moulds grow in it; and if still less, the preserve ferments.

Elevation of Temperature.—Heat is the most commonly employed and the best agent we have for disinfecting clothing, bedding, and indeed all articles to which it can be applied. If dry heat is used the temperature should be at least 150° C., and kept up for three or four hours, until it is certain that all parts have reached the required temperature. Koch recommends a jet of steam super-heated to 105° C. as being much superior to a hot chamber on account of its penetrating power. It should play upon an article for fifteen minutes. If boiling is used it should be prolonged.

Depression of Temperature.—Cold is often used to preserve articles of diet. Ice-poultices are used in surgery as dressings, especially after operations on the peritoneum and joints. Perhaps they act, in part at least, by preventing the development of organisms. Many are not killed by cold.

The most surprising differences in resisting power are found between the spore and adult forms of the same organism. The spores of B. anthracis are uninjured by

watery solutions of thymol or salicylic acid, by alcohol or glycerine; they are destroyed by chlorine- or bromine-water (2 per cent.), perchloride of mercury (1 per cent.), permanganate of potash (5 per cent.), or, in twenty-four hours, by carbolic acid (5 per cent.). They are not destroyed by drying; they withstand dry heat of 140° C. for three hours, and are not affected by the most extreme cold.

DISTRIBUTION OF BACTERIA IN NATURE.—Where are these microscopic vegetable organisms to be found? A putrid wound swarms with them. Whence do they come? 1. They may enter from the world external to the body. 2. They may exist in the healthy body, developing only under special circumstances. 3. They may be spontaneously generated under special circumstances from the elements of the tissues.

1. Earth, air, or water may be the habitat of germs external to the body.

(*a*) **Existence of Organisms in Earth.**—Portions of mould taken from the surface, and dropped into a sterilised culture-fluid infallibly infect it. Cocci and bacilli are the forms which generally develop. They are most numerous, and bacteria appear in the neighbourhood of putrefaction. All organisms are absent at a depth of one metre in soil which has not been recently disturbed, which is not formed largely of decomposing material, and into which no unusual soakage of water occurs.

Not only the earth, but all other solids in contact with air, including the surfaces of animals, have organisms deposited upon them.

(*b*) **Existence of Organisms in Air.**—That dust contains much organic matter is easily shown by combustion; and cultivation proves that some of this is living. It has thus been found that spores of moulds are the commonest forms, then bacilli and their spores, whilst putrefactive organisms are much less common. Lister notes that the result of exposing pure urine for half-an-hour in his study

in Edinburgh was the development of three moulds. Organisms of some kind exist in the air everywhere except away from all life—in mountains above the line of perpetual snow, or on the ocean far removed from land and ships. Here a sterilised fluid would not ferment if left exposed till it dried. But with life, vegetable or animal, come germs; and they increase in number as the population increases and as putrescible material becomes more plentiful. In some parts of London even it is possible to pour sterilised fluids from one flask into others with the result that but a small percentage will become turbid from the growth of germs; in other parts every flask will be infected. Precautions against such infection become necessary as density of population and imperfect ventilation increase; and it is obvious that in the hospitals of large towns such measures, to be successful, must be most stringent, for here putrefactive organisms will be comparatively numerous. A large number of the germs in air are incapable of development (Duclaux). We know that some fungi (B. anthracis) are killed by drying.

The air is kept supplied with organisms by currents which sweep them from the surfaces of objects over which they pass; the dust left as the final result of putrefactive processes is a fertile source of contamination. Perfectly still air becomes pure by subsidence of its germs.

(*c*) **Existence of Organisms in Water.** All water, except such as comes from a great depth, contains organisms. Rain-water sweeps the air and infects the soil with the germs which it carries down. All surface-water is infected from the ground through which it soaks; and too often shallow wells are contaminated by sewage, &c. River-water is exposed to all possible sources of pollution. It is scarcely necessary to add that unless the water contains sufficient organic matter to serve as food for the fungi, no multiplication will take place, and that, sooner or later, the germs will die, though perhaps not for many weeks. Many organisms in a sample of water render much organic impurity probable.

The addition of a drop of tap-water to a culture-fluid is almost always followed by the development of bacteria and ordinary putrefaction. Water may therefore be regarded as the *special habitat for bacteria*, and should not in an unpurified state be allowed to come into contact with wounds.

2. **Do Organisms Exist in the Living Body** ?—They exist in large numbers on its external (skin) and internal (bronchial and alimentary) surfaces, which are in contact with air. Inhaled with each breath, they are found in the larger bronchi; but the smaller ones and alveoli are probably free, for Tyndall has shown that the complemental air is pure by its causing a non-luminous gap in an electric beam thrown across a dark room. Further proof lies in the fact that medical empyemata communicating with the lung generally remain free from putrefaction, whilst those from external wound of the pleura always putrefy.

With food and drink many living germs are carried into the alimentary canal. All kinds of fungi swarm in the mouth cocci, bacteria, bacilli, and spirilla. They grow fewer towards the stomach, where the acid gastric juice is unfavourable to their development. Protected by their cell-membranes, some probably pass alive through the stomach. At all events, organisms reappear in the duodenum before the food has become alkaline; and the pancreatic juice swarms with organisms after impure feeding. Indeed, the products of normal pancreatic digestion, and those of ordinary putrefaction of albuminoids are practically the same. Throughout the whole intestine organisms occur, and in abnormal states of mucous membrane, or in too prolonged retention of intestinal contents, the fungi may multiply and excite irritation by the products of their action.

Lister has shown that a healthy urinary tract is free from organisms by obtaining pure urine directly from the urethra. This experiment has been widely confirmed.

But bacteria on the skin and mucous surfaces are

external to the body proper—to the tissues. That organisms are found *in* the tissues in many diseases, we shall shortly show; we have now to inquire whether they exist in the *healthy* tissues. The channels by which they may enter are—a wound of the skin (for uninjured epidermis is impervious); the bronchial and the alimentary mucous membranes. In the lung they are probably taken up like carbon particles, carried to lymphatic glands, and thence, perhaps, into the blood. Many bacteria taken into the intestine pass out with the faeces; five kinds have been cultivated and described as constantly present. The number of organisms passing through this mucous membrane varies with the number present in the food; it becomes very great when animals are fed on putrid material. Under these circumstances, living organisms may be found in the urine; as will be the case also when a large quantity of washed putrefactive organisms is injected into the circulation (W. Roberts). Many, of course, are carried to tissues other than the kidney, and are found as yellowish masses in the capillaries; they are unable to obtain food in the healthy system, and die and disappear in two or three weeks. From the above data it is probable that, under ordinary circumstances, simple organisms enter the tissues of Man in small quantity only, if at all; and that any which enter soon die, and do not reach the urine alive. Attempts have been made, upon the following plan, to prove or disprove the presence of organisms in healthy tissues. Portions of healthy organs have been removed with such precautions and placed under such conditions as to prevent their contamination from any extraneous source. The results have been contradictory. Mott and Horsley,* the latest writers on the subject, state that, with one exception out of twenty-one animals, organisms developed *when the preparations were incubated at* 37·5° C. They confirm previous observers by noting that coccus-forms precede rod-forms; that development of the latter

* Journ. of Physiol., vol. iii. No. 3.

from the former may be traced; that rods are generally found in kidney, less often in muscle, never in blood. The rapidity of development of organisms in *unincubated* specimens increased with rise of external temperature, but they do not state that such development was constant. Using the same animals, working in a room in which dust had subsided, and cleansing apparatus by heat only, Meissner kept organs in pure water free from change for two or three years. No mention is made of incubation; but it is fair to suppose that the specimens reached the same temperature as did Mott and Horsley's unincubated series. Watson Cheyne,* however, incubated organs in cucumber infusion, with a negative result. There seems no reason to believe that development here was prevented by carbolic (the spray was used), for in a few cases organisms did appear, and they always developed when the gall-bladder was included, or when bacteria had been injected twenty-four hours before death. It seems impossible entirely to reconcile the two sets of results; for the animals, their food, and the air which they breathed, were probably much the same. The rarity with which any collection of putrescible fluid in the body undergoes putrescence, though the incubation-temperature is most suitable, seems to be strongly against the existence of putrefactive fungi in healthy tissues. It is certain, however, that they may live for some hours after entry; so some "failures to preserve portions of tissue," attributed to want of care, may really have been due to the presence in them of living germs at the time of their removal from the body.

If a suitable nidus be provided for the development of organisms, they multiply and set up their characteristic decomposition. Thus Chauveau performed *histournage* of a sheep's testes before and after the injection of septic bacteria into the blood.† In the latter case, in which the testis contained organisms, it broke down into a putrid

* Trans. Path. Soc. Lond., 1879, p. 571.
† "Nécrobiose et Gangrène."

fluid and excited much inflammation around; in the former the organ underwent the fatty changes known as necrobiosis. This is the invariable course, under normal conditions; and it shows, apparently, that organisms are not present normally in the sheep's testes. Again, organisms cultivated from a case of osteomyelitis and injected into animals, caused no symptoms until their bones were injured, then osteomyelitis developed. Mere depression of the vital energy of a part, or some slight alteration of its metabolism, may therefore be sufficient to permit the development of a germ which previously died in it.

Some organisms, however, seem capable of flourishing in tissues which are perfectly healthy—*e.g.*, the poisons of the acute specifics and B. anthracis. Even here there is some very obscure difference between individuals of the same species or of closely allied species, which renders some of them suitable media for the development of certain organisms, whilst others are unsuitable. Thus some people do not appear capable of contracting the acute specific fevers; children are more subject to acute specifics than adults; Algerian sheep are inimical to splenic fever; young dogs are easily inoculated with the B. anthracis, but old ones are not. One great difficulty in the experimental study of the infective diseases of man is to find animals which are subject to them. So choice indeed are many of these organisms as to the nutritive and other conditions under which they will develop, that they are satisfied only in certain tissues or fluids of the body; some multiply in the blood, others in lymph, some in bone (osteo-myelitis), others in the cerebro-spinal meninges (epidemic cerebro-spinal meningitis), and so forth.

To sum up these long paragraphs.—Organisms innumerable exist in air, water, earth, and on all objects exposed to air; on the skin and on those mucous surfaces which are in contact with air. Experience shows that putrefaction after death begins in the abdomen, spreading from the alimentary canal to the organs round about

it. Organisms probably pass constantly through the pulmonary and intestinal mucous membranes, but in small number; and such as ordinarily thus enter the tissues are unable to develop, so long as the latter are healthy. The life of such fungi among the tissues is short. It seems to be a very rare thing for them to reach the urine alive. Occasionally an organism which is not universally present, and which can develop in living tissues, enters the tissues. The recipient of such organisms is in more or less danger of disease. The great majority of mankind afford a suitable nidus for the development of some fungi; thus few are immune to the vaccine-virus. All organisms perhaps flourish best in tissues of which the vitality is impaired; some probably cannot develop unless this is the case; and still another group cannot multiply in living tissues at all. Two great divisions (clinical) of organisms are thus obtained:—1. The **Pathogenic,** or those which can invade and multiply in living tissues, giving rise almost invariably to disease. 2. The **Non-Pathogenic** or **Simple,** which can develop only in dead tissue, and are therefore found chiefly on the surface of the body, where sloughs and discharges are common. The most important of these is the Bacterium termo, the cause of putrefaction. It is a very rare occurrence for this fungus to find its way alive to an internal slough or putrescible effusion, as it did in Chauveau's experiment.

Spontaneous Generation.—The possibility of organisms originating *de novo* from the molecules of decomposing tissues must be mentioned, but cannot be discussed. The great majority of observers are agreed that there is no evidence of its occurrence at the present day. They hold that, if a fluid be thoroughly sterilised, and placed under such conditions that no organisms can enter from without, no organisms will develop.

We conclude, therefore, that organisms found in a putrid wound have entered it *from without;* and that the same is true of fungi found in pathological lesions within the tissues, the organisms having entered by a wound or

mucous surface. For the present, at least, we must adhere to the belief that neither living organisms nor their spores exist normally in the tissues; and that they are never eliminated alive by an excretory organ or by a wound.

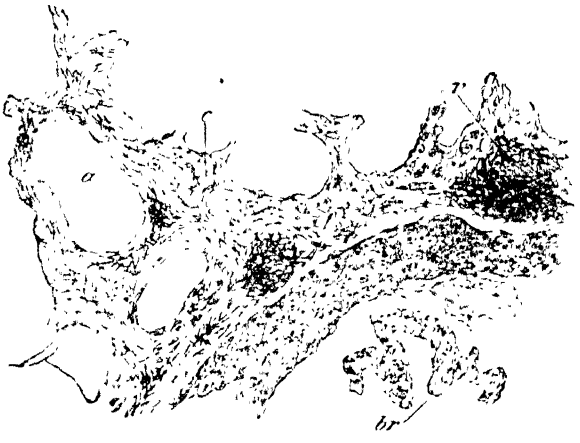
This is of fundamental importance in surgery. If the Bacterium termo could enter a wound from the side of the tissues, aseptic treatment would be impossible. As it is, we are sure that, if we allow no loophole for the entry of germs from without, our wounds will remain sweet. Patients are thus saved from the danger of septic intoxication, and also almost certainly from septic infection and pyæmia; for the fungi giving rise to the latter diseases find in septic wound-discharges a favourable nidus, whence they readily invade the tissues, but they very rarely enter the body by any other channel. Attention to general hygiene is the only way at present known to prevent invasion of the system by fungi which cause "medical" diseases. Once organisms have gained access to the tissues, it is extremely difficult to destroy them without also destroying the tissues. Improvement of the general health probably often enables the tissue-elements successfully to resist invasion.

ORGANISMS IN LIVING TISSUES.—MODES OF SPREADING.—EFFECTS.—Having obtained an entry, **pathogenic fungi** may remain about the spot at which they entered, or they may spread by continuity of tissue with all degrees of rapidity, or they may pass along lymphatic vessels to the nearest glands or even into the blood, or they may at once enter the circulation and be carried all over the body. B. tuberculosis, for example, has been seen entering vessels of all kinds; M. erysipelatis grows in the lymphatic capillaries of the skin, and so on. Everything depends upon the life-requirements of the fungus, which may be satisfied only in lymph or in blood, or in some particular tissue. They are not uncommonly found within cells—*e.g.* white corpuscles, giant-cells; and it is possible that white corpuscles destroy them. In the tissues they grow always along lines of least

resistance, as is best seen when the cornea is inoculated with fungi; they then run along the lymph-spaces in which the cells lie, forming a characteristic figure called the "Pilz-figur."

Once in the blood-stream they are swept to any part of the body. They can be seen in the plasmatic zones of veins in transparent parts. Where they will stop is probably decided by the relation between the mass they

FIG. 119.



Mouse's Lung; vessels plugged with Bacilli anthracis.—*a.* Alveolus. *v.* Vein full of bacilli. Capillary, also full. *br.* Bronchus. × 500, slightly reduced.

form and the size of the vessels; they may or may not be able to develop where they happen to be arrested. Some organisms can multiply in moving blood, but all are favoured by rest. When they have come to a standstill, the germs may remain within the vessel or pass out into the surrounding tissues. Surrounded by stationary food, they now set up chemical changes in it, which render it more or less irritant to the neighbouring tissues, and

capable of exciting all changes from a very chronic inflammation (tubercle) up to suppuration (pyæmia) or direct necrosis. At the same time some of the products are absorbed, and often give rise to fever. These are the two chief modes of action; but fungi will produce some effect by abstracting nourishment from their host, and, perhaps, also by plugging a large number of the vessels of some important organ—as the lung. The accompanying figure, showing the Bacillus of splenic fever in the vessels of a mouse's lung, gives an idea of the extent to which this process may be carried. (Fig. 149.) The specimen was kindly given by Mr. Horsley.

SPECIFIC CLASSIFICATION OF BACTERIA.—Authorities differ as to whether this is possible. We have as yet nothing like complete data for the purpose; indeed it cannot be said that we know certainly the whole life-history of a single bacterium. All apparently multiply by division; in many spore-formatino also is known; but it probably occurs in others in which it has not yet been seen. As reproduction affords at present no ground for subdivision, we must turn to morphological characteristics —viz., form and size, for no structural difference can be made out. Are these two points sufficient to serve as the basis of a classification?

Cohn maintains that there are orders characterised by distinct forms, which they adhere to throughout their whole life. Some are spherical, others rod-shaped, others twisted like a screw. Specific differences are established by minor differences in form, such as rounded or sharply truncated ends of rods, variations in size and in mode of growth, and by the discovery of the physiological action of the organism, each one having some special feature in this respect. Thus two spherical bacteria of the same size may be distinguished by a totally different physiological action; and this will necessitate their being classed as distinct species. As an analogy Cohn points to the close naked eye and microscopic resemblance between the sweet and bitter almond, the physiological

actions of which are so very different; and Virchow, in the same sense, alludes to the impossibility of distinguishing between the cells of the early embryo, though their potentialities are so various. Koch supports this view strongly; for he has been able to cultivate fungi of easily recognisable form through many generations, and has been able to note no change, either morphological or physiological, such as would lead him to suppose that it is possible for a given form with a well-defined physiological action to pass into another form having a different action. Koch thinks that no alteration in food or in physical conditions will transform a micrococcus into a bacterium or bacillus, and that there is no evidence of the apparently slighter change from a harmless non-pathogenic bacillus (B. subtilis) into a virulent pathogenic one (B. anthracis) having been effected by these means. Cohn and Koch may therefore be cited as believing that specific classification of Schizomycetes is possible, and that the different species which they describe are immutable.

On the other hand, it is believed that Cohn's divisions are merely developmental forms of one (Coccobacteria septica, Billroth), or a few undetermined species (Nägeli). The arguments on this side are:—

1st. That in successive cultivations, especially in different media, the forms developed have varied greatly from the original, assuming in succession the shapes characteristic of Cohn's orders; and at the same time their physiological activity has changed equally. This is, of course, a direct contradiction of Koch's statement and may be true; but it must be remembered that the method employed (successive cultivation) is one in which error is easy. In fact it is far easier to fail than to succeed; so the suspicion that the cultivations have become contaminated by other organisms arises. It must, however, also be borne in mind that many of the observations which support the above statement were made by men of the highest skill.

2ndly. Different forms of bacteria are found taking

part in the same decomposition (*e.g.*, putrefaction). This shows simply that several different organisms are capable of living in the same fluid; the process is a complex one, and the products are the result of the life-actions of different forms; it does not show that different forms develop from one species.

3rdly. The same form may be found associated with the most different chemical changes. Thus micrococci, indistinguishable from each other by form or size, occur in relation with diphtheria, erysipelas, smallpox, pyæmia, infective osteo-myelitis, and many other diseases. They cannot be the same if they are the cause of these maladies; but that similar forms may be specifically distinguished by their physiological activities has already been shown (p. 498).

4thly. Coze and Feltz, Davaine, and others, produced an artificial septicæmia by injecting putrid fluids, containing many forms of bacteria, into rabbits, and found that the virus increased as the disease was transmitted from animal to animal; so that in the twenty-fifth transmission of a series, Davaine produced fatal septicæmia with one trillionth of the original dose of one drop. But this apparent increase in virulence was due to neglect of a control-experiment made by taking the smallest quantity possible at an early stage. Davaine himself thus found that no increase of virulence occurred after the second or third generation; and Koch shows that even this was due to greater purity of the organism inoculated, forms other than that specific to the disease having rapidly diminished, whilst the specific one increased and multiplied. Similar increase in physiological activity produced by cultivation has been alleged to occur in other organisms, and has been similarly explained.

5thly. Buchner states that by cultivating the non-pathogenic, hay-bacillus in meat-infusions, and in unsterilised blood, he made it "savage," and converted it into B. anthracis; and that by a converse process he converted B. anthracis into B. subtilis. The experiments have been

repeated with negative results by Koch, who points out the probable flaws in Buchner's experiments, and, more recently, by Klein.

6thly. By cultivating B. anthracis at 42°–43° C., Pasteur succeeded in so "attenuating" the virus of splenic fever, that when inoculated upon sheep it caused little or no illness, but conferred upon them immunity from splenic fever; of fifty sheep, twenty-five vaccinated with the attenuated virus, all lived, twenty-five unvaccinated all died when inoculated with the virulent poison. This result was twice obtained. Other experiments, though less successful, have been, on the whole, confirmatory. But Koch, Löffler, and Chauveau, have not succeeded in attenuating the virus or in conferring any certain protection. Perhaps this is owing to the fact that Pasteur has not published an exact account of his method of attenuating the poison. As regards Rodents, Klein failed wholly to produce immunity; so long as the B. anthracis acted at all it produced splenic fever. By similar cultivation at 42°–43° C., or by leaving the organisms of chicken cholera in chicken broth exposed to air for 8–10 months, they were similarly attenuated, and protected the fowl for perhaps a year from attacks of the disease (Pasteur). Quite recently, Pasteur has stated that he is able similarly to vaccinate against hydrophobia. The analogy of these processes with vaccination is destroyed by the absence of proof that vaccine is smallpox poison attenuated by cultivation in a cow. In the above cases the physiological action of the fungi must undoubtedly be modified by the treatment they undergo, but the modification is not such as to prevent a specific classification.

This is the experimental evidence as to the **mutability of bacteria**. At present the balance is decidedly against it, but Koch himself recognises that his experiments do not prove its impossibility. Like all other organisms, these unicellular beings must have more or less power of adapting themselves to altered surroundings, and will be

modified by the latter; the question is whether marked modification can be thus produced within periods which can be covered by observations. Koch's experiments are sufficient to show that many fungi, at all events, preserve unaltered through long series of cultivations their inherited characteristics.

Looked at from the clinical point of view, every one feels that the best marked group of infective diseases—the specific fevers—must have an unvarying, a specific cause. Most observers believe that these diseases never arise except by infection from a previous case. Assuming the virus to be a fungus, they admit that it must at some time have acquired the physiological action which enables it to produce a certain disease; but they hold that there is no evidence that harmless fungi do at the present time ever acquire such powers. Isolated communities remain free from such diseases for centuries until a case is introduced among them; then it spreads with the utmost rapidity. In 1520 a negro, covered with smallpox pustules, was landed on the Mexican coast, where the disease was not yet known; three and a half millions are said to have died of it. In 1846, measles was introduced from Copenhagen into the Faroe Islands, and almost every one suffered. Similar facts concerning other acute specifics are given by Sir T. Watson, in *Nineteenth Century*, No. III. Murchison and others believed that typhus and typhoid might originate *de novo*, being filth-begotten; but the conditions of life in slave ships and Arctic winter-houses are as unsanitary as ever they were in our gaols when typhus was endemic in them—yet no typhus occurs. As to the origin of typhoid from sewer-gas, Continental towns show that exhalations of it may be intense and prolonged without ever generating typhoid.

The poison of the most infectious diseases has obviously so great a power of spread by air, food, clothing, &c., that it is almost impossible to find a case in which the possibility of infection from a previous case cannot be shown. The less infectious kinds have, therefore, been turned to

by the advocates of the *de novo* origin. Many cases of supposed spontaneous origin of diphtheria are recorded; and a urethral discharge like gonorrhœa, in symptoms and communicability, may, it is said, be contracted from a woman suffering from any foul discharge—not gonorrhœal. But it is quite possible that urethral discharges may be excited by infective irritants other than the gonorrhœal poison. With regard to the so-called Hospital Diseases—pyæmia, septicæmia, hospital gangrene—there is, perhaps, evidence of some change from non-pathogenic to pathogenic organisms. How otherwise is it to be explained that, when a new building, which has never before contained wounded, is taken in time of war as a hospital, these diseases break out so soon as crowding of the wounded reaches a certain point, whilst they do not attack patients in tents close by? Can we suppose that the specific causes were present in the building? or do not the facts tempt to the belief that ordinary bacteria acquire pathogenic properties by cultivation under the conditions brought about by overcrowding of the wounded? The state of atmosphere produced in the building would seem to be analogous to the "epidemic influence"—that influence which causes infective diseases every now and again to become widely epidemic. From the clinical standpoint, therefore, it would seem that but little evidence is forthcoming in favour of the mutability of bacteria; but the question must be regarded as entirely *sub judice*.

It will be seen that, by origin *de novo*, a germ-theorist understands—not the spontaneous development of an organism, but the acquisition under suitable cultivation of pathogenic properties by a non-pathogenic fungus.

The acute specific diseases, to which allusion has so often been made, are now regarded as forming a class in the much larger group of **Infective Diseases**. These may be defined as diseases due to the action of a poison or virus which has the power of invading and multiplying in living tissues. They may be local or general, *i.e.*,

the virus may be able only to invade the tissues for a greater or less distance about its point of entry, or it may be able—either directly by multiplying in the blood, or indirectly by throwing into it the products of its action in the tissues—to excite the tissues in general to increased metabolism (fever), and perhaps to lodge in other tissues and excite fresh foci of disease.

These diseases are divided according to certain characteristics of the virus:—

1. **Contagious.**—These are communicable only from individual to individual; the poison runs its whole course of development in the body. Scarlet fever, measles, small-pox are examples. They are frequently epidemic.

2. **Miasmatic.**—These are endemic diseases of which malarial fever is the type. This disease is not communicable from man to man; the poison which causes it develops outside the body, having no relation to a previous case of ague.

3. **Contagio-miasmatic.**—In this class are placed certain diseases which seem to be derived always from a previous case of the disease, but not directly; the poison has to go through some change external to the body. The best examples are typhoid and cholera. There is doubt as to what constitutes the peculiarity of this group. The hypothesis of an essential change taking place external to the body, originated with the Munich school. But Pettenkofer has abandoned it, and thinks that these diseases differ from the miasmatic simply in being transportable by man from their seat or seats of origin.

4. There would seem to be another set of diseases—**septic**—the poisons of which may be derived from many putrid infusions. When the disease has once been started in this way, it can be transmitted directly from individual to individual indefinitely.

It will be remembered that, having pointed out the analogy which exists between fermentation and infective disease, we considered the views which have been put forward as to the etiology of fermentation, and concluded

that the germ-theory was almost certainly the true one. It seems impossible to furnish absolute proof of it, for it is impossible to cleanse the germs so thoroughly as to be sure that no particles in a state of "motor decay" are added with it to a test-fluid. The facts, however, that the particles in a state of motor decay have never been demonstrated apart from organisms, and that the properties of the cause of fermentation appeared to be those of a living thing, render it, as has been said, almost certain that organisms stand to the process of fermentation as cause to effect. There is, therefore, on the strength of the above analogy, a *primâ facie* case in favour of the germ-theory as applied to the infective diseases. And it will be found upon examination of the evidence yielded by actual observation of these diseases, and by experiments upon animals, that the demonstration of the causal relationship of organisms to them is in some cases as complete as it is in the case of fermentation, although in the great majority the proof is still more or less doubtful.

To prove that a micro-organism is the cause of a disease, it is necessary:—

1. To find the same organism recognisable by its form, mode of growth, or products, constantly associated with the disease, at least in its earlier stages; and in sufficient numbers to account for the symptoms.

2. To produce the disease in other animals by inoculating them with material containing the organism taken from diseased animals.

3. To make "pure" cultivations of the organism through several generations; and, when it may reasonably be supposed that all else taken from the animal which yielded the virus has disappeared, to inoculate other animals with the cultivated organism and still to obtain the same disease.

The demonstration of a well-characterised organism in constant association with a disease is now by many taken as almost equivalent to proof that it is the cause of the morbid process. For it is, in most cases, impossible to experiment on Man, and frequently no animal can be

found which suffers from the disease under investigation. Consequently, the proof cannot be carried beyond the first stage. This, however, is no proof at all to those who believe that under certain circumstances a certain form of organism will develop spontaneously; nor is it satisfactory to others who think that, when a nidus favourable to a certain organism exists, that organism is sure to drop into it.

The amount of patience and skill necessary to carry on an investigation of the above kind can be appreciated only by those who have worked at the subject. They are not surprised that so few diseases have been thoroughly investigated. In the case of man, the difficulty of obtaining material in the early stages of diseases, and sufficiently soon after death must also be taken into account. Until quite recently, too, the methods employed were wholly inadequate to the discovery of many kinds of fungi. At first there was unaided microscopic examination only, and with inferior glasses; the detection of all fungi, under these circumstances, was very difficult, and often impossible. A considerable step was made when v. Recklinghausen, in 1871, pointed out the uniform size and the resisting power of micrococci against dilute acids and alkalies and glycerine as a means of diagnosis between them and fatty and albuminoid particles. But progress has been much more rapid since the introduction by Weigert of the aniline dyes as stains for organisms, and by Koch of many improvements in the mode of examining specimens and of carrying on pure cultivations. Details of these processes will be given on p. 533.

THE SCHIZOMYCETES.

We shall now, adopting Cohn's classification, give the orders, genera, and some of the species of the Schizomycetes, and state the grounds for believing that certain of them are causally associated with disease.

Order 1. **SPHÆROBACTERIA or MICROCOCCI.**—These are round or oval cells, generally ·5 to 2 μ in diameter,

300), which may be straight or wavy. They often occur also in colonies and zooglœa-masses. The chains only seem sometimes to have slow spontaneous movement. They differ among themselves in form, size, mode of grouping, and physiological action, and thus are established genera and species. Though often found in putrefying fluids, they are not the cause of putrefaction.

There are two genera:—Micrococcus and Sarcina.

1. **Genus Micrococcus.**—Cohn arranges the species of Micrococcus in three groups:—pigment-forming, fermentative, and pathogenic.

(*a.*) **Pigment-forming.**—Uncoloured themselves, they form in contact with air, slimy films of various colours. They are frequently seen on bits of boiled potato. The colour does not vary with the soil, but is specific to each form. The species are:—M. prodigiosus (red), the cause of the "bleeding" host; M. luteus, aurantiacus, chlorinus cyaneus—the cause of blue pus—and violaceus.

(*b.*) **Fermentative.**—M. ureæ, the cause of the ammoniacal fermentation of urine, which it enters from the air. Urine obtained pure and exposed only to pure air will keep acid for years. The change effected in the transformation of urea into ammonic carbonate is said to be due to the action of an unformed ferment secreted by M. ureæ (Musculus*) which must be indiffusible, for the urine in an excised bladder does not putrefy even if placed in putrid urine. The change often occurs in urine contained in the living bladder, and may extend up to the pelvis of the kidneys with the most fatal results (suppurative nephritis, p. 392). M. ureæ is rather large (2 μ) and occurs singly or in chains.

(*c.*) **Pathogenic.**—The absence of distinctive form is a great difficulty in the carrying on of "pure" cultivations, and in the demonstration that a specific coccus is the cause of a disease. Cocci are more frequently associated with diseases than any other form of fungus.

Micrococci (Fig. 150, 2) have been found in large numbers

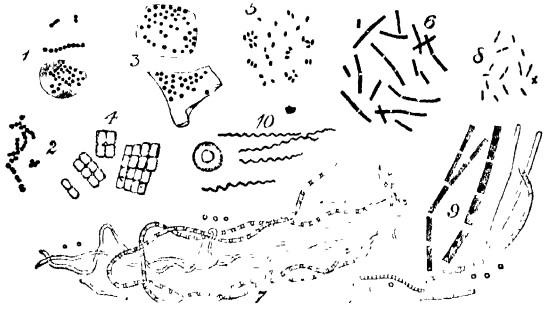
in the secondary deposits of **Pyæmia** (Rindfleisch, v. Recklinghausen, and many others). It has been shown that the unhealthiness of the wound is in proportion to the number of zoogloœa masses on its surface, and the severity of the disease to the number of cocci in the blood (Birch-Hirschfeld); the cocci have been traced from the wound into connective tissue interspaces and into a vein (Klebs). Cultivation-experiments are still needed; inoculation of animals from man has repeatedly failed. By injecting a putrid infusion of skin Koch obtained an infective disease in rabbits like pyæmia in man; a micrococcus was constantly present in the blood. The disease was transmitted from animal to animal several times (p. 473).

With putrid blood spreading gangrene, with a specific coccus growing in chains, was produced; and in rabbits, abscess spreading from the seat of inoculation, was produced with clouds of very small cocci (·15 μ) in the wall; each was locally infective, and was transmitted several times. A septicæmia of rabbits, with a characteristic oval coccus, was also produced. In these cases there seems no loophole for doubt that the organisms really caused the diseases. Many organisms were at first injected, one only developed after inoculation, and each transmission was therefore a pure cultivation. The poison evidently multiplies; and as we have rejected the physical explanation of this increase (p. 479), we have only the vital theory left. Every student should read Koch on "Traumatic Infective Diseases," where a full account of the above maladies is given.

Micrococci are constantly present in the pus of **acute abscesses** (Fig. 150, 1); in chronic they are not found. Many observers have noted this. Ogston found that pus from acute abscesses in man caused acute abscess in animals when inoculated upon them; the disease could be transmitted from animal to animal; cultivation of the cocci of the original abscess succeeded in eggs, and inoculation of the cultivated organisms again caused abscess. The

same litter proved much more resistant than others. In some cases well-marked septicæmia occurred, the symptoms in mice being such as were described by Koch. Micrococci were then found in the blood, though never

FIG. 150.



1. Micrococci from an acute abscess—some in a pus-cell. 2. Micrococci from secondary suppuration in elbow (puerperal fever; lent by Mr. Horsley). 3. Micrococci from gonorrhœal pus, in cells. 4. Sarcina ventriculi. 5. Bacterium termo. 6. Bacillus anthracis, from blood of mouse (lent by Mr. Horsley). 7. Chains from cultivation of B. anthracis; some bearing spores (after Duclaux). 8. Bacillus of typhoid, from a mesenteric gland (lent by Dr. Gibbes). 9. B. malariæ: dichotomous division, parietal spore-formation, jointed and unjointed threads which appear in cultures and fine spores; × one-twelfth, oil-immersion, Zeiss (after Klebs and Tommasi Crudeli). 10. Spirilla of relapsing fever, and red corpuscle (after Vandyke Carter). All × 500 except B. malariæ.

in very large number, apparently. Ogston concludes that all acute suppuration is due to micrococci; and that the same organisms may under unknown circumstances give rise to septicæmia.*

Erysipelas.—Micrococci have often been described in

erysipelatous skin, especially at the spreading edge; v. Recklinghausen and Lukomsky* showed that they occupied the lymphatic channels and spread along them (hence the name—infective capillary lymphangitis). Orth produced typical erysipelas in a rabbit by subcutaneous injection of the fluid from an erysipelatous bulla; with œdema fluid from this animal he successfully inoculated another; the fluid and affected skin contained cocci in large numbers. Orth cultivated the fungus, and produced erysipelas by injecting it. Last year Fehleisen (D. Ætiologie des Erysipels) found numerous cocci in chains constantly present in bits of skin excised from patients having erysipelas; they lay in the lymphatics chiefly of the superficial part of the corium and in the subcutaneous fatty tissue, never in blood-vessels. They had excited round-celled infiltration about them. The cocci were cultivated upon gelatine through fourteen generations in two months; eight out of nine rabbits now inoculated suffered from the disease; six out of seven inoculations upon man were equally successful. The incubation was 15–60 hours; then followed rigors, fever, and typical rash. The disease was severe in two cases. Immunity, if conferred at all, lasts less than two months. Three per cent. solution of carbolic acid, one per cent. of perchloride of mercury stopped the growth of the fungus.

Diphtheria.—In the membrane characteristic of this disease are found numbers of micrococci with other organisms. The cocci have been found also in the tissue upon which the membrane lies, and have several times been traced thence along the lymphatics to the nearest glands; miliary deposits of them have been found also in the heart, liver, kidneys, and other organs, closely resembling those of pyæmia, having even a similar brownish colour. Their occurrence probably explains the complications, especially albuminuria, which are often met with.

* Virch. Arch., vol. lx., p. 418.

Trendelenburg infected the bronchi of rabbits with bits of membrane, and Hüter the conjuctiva. Klebs and Letzerich cultivated the organisms, but rabbits inoculated died very rapidly, perhaps of septicæmia, without the occurrence of membranes. Löffler has a paper in the recent volume of the Mitth. a. d. k. Gesundheitsamte in which he describes a bacillus as the specific organism of diphtheria. The possible origin of the disease from a miasm or fungus growing outside the body has been alluded to.

The disease is probably primarily local, its seat being most commonly the throat. The lesion here is comparable to the primary sore, not to the sore throat, of syphilis; for in cases in which the seat of inoculation is a wound, no affection of the throat appears, as was noticed in cases occurring in the wards of the Children's Hospital when diphtheria-cases were not isolated. It is believed by many that these cases of obvious diphtheria of wounds pass on the one hand into Hospital Gangrene, and on the other into croup of granulations. It is said that endemic pharyngeal diphtheria goes with endemic wound-diphtheria (Huter). Proof of the identity of these processes is wanting. Membranes of diphtheritic aspect appear occasionally on almost all mucous membranes, but without any symptoms of diphtheria. Their occurrence shows simply that irritants other than the diphtheritic virus can produce that form of necrosis and quality of exudation which make up the true diphtheritic membrane (p. 288). Simple irritants may produce similar membranes (p. 377); they contain cocci, which have fallen on to them.

Gonorrhœa.—Neisser, in 1878, described a large micrococcus peculiar to this disease. (Fig. 150, 3.) He was able to distinguish it from ordinary cocci by its size, by the distance between the individuals in the groups, about equal to the diameter of a coccus, and by their occurrence upon the surfaces of cells; and he used it as a means of diagnosing gonorrhœal discharges from urethra, eye, &c. He cultivated it, but failed in his inoculation-

experiments. These have been successfully carried out by Bockhardt.* He injected a fourth cultivation into the urethra of a general paralytic, and produced a purulent discharge. The man died of pneumonia ten days later, and an examination of the urethra led Bockhardt to believe that the cocci probably pass through the epithelium into the lymphatics of the fossa navicularis, where they excite lively inflammation. They enter into white corpuscles, and pass with them into blood-vessels, where they die; or they come away in the pus.

Pneumonia.—Klebs described a micrococcus as present in pneumonia,† and was confirmed by Koch‡ and Friedländer§ who demonstrated the constant presence of the organisms in great numbers in the early stages, not only in the exudation, but also in the lymphatics of the lung. Friedländer‖ now states that he has cultivated the coccus in blood-serum and gelatinised meat-infusion and on potato. Diffused in distilled water and injected into the lung and pleura of rabbits, they produced no effects; but thirty-two mice died without exception, and generally in eighteen to twenty hours. The lungs were very red and almost universally solid, and the spleen was enlarged; both organs contained the characteristic cocci, which were present in considerable numbers in the blood, and in enormous numbers in fluid which occupied the pleura. Guinea-pigs were more refractory to the poison, and only one dog of five suffered.

Inhalation-experiments were made by spraying water charged with cocci for five minutes into the cages of mice; three of ten developed pneumonia. The effect of chill was not excluded.

* Sitz. Bericht d. Phys. Med. Gesell. Wurzburg: 1882.

† Arch. f. Exp. Path., iv.

‡ Mitth. a. d. k. Gesundh. 1881.

§ Virch. Arch., vol. 87.

‖ Fortschritte d. Med.; abstract in *British Medical Journal*, p. 174, vol. i., 1884.

The cocci are large, oval, stain best with Ehrlich's gentian-violet, and have round them a peculiar capsule of mucin (Friedländer), which is not, however, constant. Epidemics of pneumonia have often been described, and complete proof of the view that it is an infective disease seems to be close at hand.

Salvioli and Zaslein* confirmed some earlier observations of Friedländer. They found the coccus in the blood and in blister-fluid of pneumonic patients, and in them only. They cultivated it, and found that, when injected, it produced pneumonia and fibrinous pleurisy in rabbits, whilst the culture-fluid alone did not do so.

Measles.—This disease has been given by inoculation of the healthy with the blood of the sick. Organisms have been found in the breath, in the blood, and in the skin, lungs, and liver. They are large, highly-refracting, round or fusiform bodies which remain unstained by carmine.†

Keating‡ says that he examined two series, each of eight cases, and found a special coccus constantly present in the papules; it was demonstrable in the blood in severe cases only. Here it either occupied the interior of leucocytes or performed swirling movements round them. The prognosis is bad if cocci are seen in the blood.

Vaccinia.—Cocci, present in the vaccine-vesicle, have been cultivated by Godlee and others; but vaccination could not be effected with the cultures. Success would eliminate the possibility of conveying any disease other than vaccinia by the inoculation. Quist§ states that he has vaccinated successfully with cultures. He says that both cocci and bacilli are constantly present in the vesicles, and that the latter are developed from the former.

* *Ctbl. f. Med. Wiss.*, p. 721, 1883.

† Braidwood and Vacher, *British Medical Journal*, vol. i., p. 77, 1882.

‡ *Phil. Med. Times*, xii. No. 384. 1882.

§ *St. Petersb. Med. Wochenschr.*, No. 46, 1883.

They are purely aërobious, and grow in serum diluted with water containing some glycerine to prevent evaporation. After 8–10 days, superficial flakes, and then a precipitate, of cocci form. Vaccination, with material taken 1–1½ cm. from the point of inoculation, are successful. In one case the cultivation was carried through three generations.

Cerebro-spinal Meningitis (Epidemic).—Marchiafava and Celli* found cocci constantly in the exudation, generally as diplococci; probably smaller than gonorrhœal organisms. They are not present in the organs generally, but are found in groups in the pia mater.

Micrococci have been described also in **Typhus**† (actively moving, dumb-bell cocci in blood in all cases [twelve], and plugs of them probably in lymphatics in each of six hearts examined), **Scarlatina**,‡ **Variola**,§ **Infective Periostitis, Endocarditis**‖ (not only ulcerative), **Acute Yellow Atrophy**¶ of the liver (early stage), **Whooping-cough**,** and **Dysentery.**†† Pasteur has proved that a fatal disease of silkworms, **Pébrine**, is due to the action of a micrococcus (M. bombycis). The disease is hereditary, and the coccus is found *in* the eggs.

II. **Genus Sarcina.**—A micrococcus which divides in two diameters at right angles to each other, is often found in vomit from stomachs dilated from pyloric obstruction, in cases of dyspepsia from chronic catarrh (Sarcina ventriculi), in the bronchi and deeper parts of the lungs in chronic inflammatory diseases, and in the urine (S. urinæ); it has been seen also in abscesses and in blood. Single cocci may be seen, but the majority form square groups of four,

* *Gazz. degli ospitali*, No. 8, 1884—quoted from *Cbl. f. Klin. Med.*
† Mott, *British Medical Journal*, vol. ii. 1883, p. 1059.
‡ Pohl-Pincus, *Cbl. f. Med. Wiss.*, 1883, p. 641.
§ Weigert, *Anat. Beitr. z. Lehre v. d. Pocken*, 1874.
‖ Koch, Mitth. a. d. k. Gesundheitsamte, 1881.
¶ Dreshfeld, *British Medical Journal*, 1883, vol. ii. p. 1057.
** Bürger, *Berl. Klin. Wochenschr.*, 1883, No. 1.
†† Prior, *Cbl. f. Klin. Med.*, No. 17, 1883.

or some multiple of four (Fig. 150, 4). S. ventriculi is larger than S. urinæ, or than the fungus of this shape occurring in the lungs. The presence of sarcina in the stomach does not cause it to appear in the urine or elsewhere. It is extremely difficult to get rid of the fungus, when once established. The nature of the decomposition to which it gives rise is unknown.

Order 2.—**MICROBACTERIA.**—One Genus—**Bacterium** (the name "bacteria" has unfortunately been applied to the whole class). The tendency now is to limit the name to cylindrical or oval cells, of which the length is not more than twice the breadth, which multiply by transverse division, are frequently seen in pairs and in zoogloœa-masses with much intercellular substance, but never in long chains. In cross section the zoogloœa-masses look like coccus-colonies, but rods may be seen at the edge. Spores have not yet been demonstrated. These fungi may be actively mobile or motionless.

Pigment-forming.—*B. synxanthum* occurs in yellow milk, the colouring matter being soluble in water; *B. œruginosum* in greenish-blue pus.

Fermentative.—*B. termo* (Fig. 150, 5) is the most important species, being apparently the cause of putrefaction (Cohn). It is cylindrical, with rounded ends, 1–2 μ long, often in pairs, and has a trembling movement. It is non-pathogenic, being unable to exist in living tissues; part of its action is due to the formation of unorganised ferments; its products closely resemble those of pancreatic digestion; many of them are fever-exciting, though one—*sepsin* (Bergmann)—which has been crystallised out, has been given special prominence. The non-infective disease, septic intoxication, is due to the absorption of the poisons formed by B. termo.

B. lineola—like, but much larger than, B. termo, often occurring with it, but also in fluids free from putrefaction.

B. lactis.—The cause of lactic fermentation of milk (Lister).

Pathogenic.—A motionless bacterium of small size,

lightly constricted in the centre, has been shown by Pasteur to be the cause of the disease known as "chicken-cholera," though no symptom suggests a resemblance to cholera.

Order 3.—**DESMOBACTERIA.**—Rods of which the length is more than twice the breadth, and generally considerably more, so that these fungi are slender. They multiply by transverse division, and often grow into long, jointed, but unbranched filaments, not constricted at the joints. Formation of spores has been detected in some species. Swarms of bacilli are common, but they are rarely imbedded in zooglœa. There are two genera:—**Bacillus**, rods straight; **Vibrio**, rods wavy.

Pigment-forming.—B. syncyanum occurs in blue milk.

Fermentative.—*B. subtilis.*—Found in hay-infusions and many other organic substances. Very delicate, actively-moving rods, having a cilium attached at each end. When nourishment fails, they become motionless, and bright, oval spores form in their interior. It is an aërobious fungus.

B. butyricus.—The cause of butyric fermentation. Rods vary from 3–10 μ in length; slender at first, they become plumper, and the shorter ones appear spindle-shaped; oval spores form in their interior. The rods may grow into long or short chains, and in the latter condition quite lose mobility. Oxygen kills the bacillus (Pasteur).

Pathogenic. — Splenic Fever.—The *B. anthracis*, found in this disease is the best known of all the parasitic fungi. Its life-history was worked out by Koch.* In blood from the spleen of animals dead of splenic fever are found enormous numbers of rods, 5–20 μ long by about 1 μ broad, straight, with slightly concave ends and motionless (Fig. 150, 6). In a suitable culture-material (the blood of the dead animal is one), with a

plentiful supply of oxygen, and a temperature between 15° and 42° (25°—30° being most favourable), the rods grow into very long filaments (Fig. 150, 7); in these, round highly refracting spores form at short and regular distances; the filaments now break up, and the spores are set free. Under favourable circumstances these grow into bacilli. In living animals, long filaments and spores are never found; the rods multiplying solely by division. The rods exist in enormous numbers in the capillaries, especially those of the spleen, lungs, liver, kidneys, and mucous membrane of the intestine. Numbers leave the body in the urine, fæces, and blood flowing from the nose and mouth of the animal before it dies; thus the grass is covered with the fungi. In bodies buried at a depth of one metre, oxygen and a suitable temperature are wanting, so no development of spores occurs, and the bacilli soon die. Pasteur's belief, that spores do develop under these circumstances and are brought to the surface by earthworms, is erroneous (Koch). As to the mode of infection—Pasteur says that the mouths of animals are wounded by siliceous grasses, and the cuts inoculated with bacilli or spores, a view supported by the frequent swelling of the cervical glands in sheep; but these animals and man are frequently infected by insects which bite them on the face. Koch thinks the intestine is the commonest seat of infection; Klein, however, records a case in which one mouse ate most of another which had died of splenic fever, without ill results. In warm, marshy districts, the bacilli form spores plentifully; these are carried by floods to meadows where anthrax may not have occurred previously.

In Man, malignant pustule is due to inoculation with B. anthracis; in this country, generally, from wool or hides brought from countries where the disease is endemic. Some time after the appearance of the pustule, as a rule, general symptoms appear, bronchitis or diarrhœa being common. Davies-Colley* found numerous bacilli in

* *Path. Soc. Trans.*, 1883, p. 291.

serum pressed from an excised pustule, and in the sputum, urine, fæces, and sweat. The patient recovered; but though free from symptoms he was still eliminating in his urine a few bacilli a month after excision of the pustule. In some cases there is no superficial lesion, and the symptoms may be those of acute septic poisoning, or chiefly pulmonary or intestinal (Woolsorter's Disease). Perhaps the predominant symptoms indicate through which mucous membrane infection took place.

B. anthracis is constantly present in splenic fever, and ultimately in enormous numbers. Blood of the fœtus of an animal with splenic fever, which contains no organisms, does not produce the disease; whilst blood containing bacilli capable of development or spores, always does in suitable animals. The bacilli may be separated by filtration, and washed with distilled water, alcohol, ether, and then dried—they still cause splenic fever. Pure cultivations may be made through fifty generations, with the same result. It never gives rise to any other disease. If this is not proof that B. anthracis is the *cause* of splenic fever, the belief that itch is due to acarus scabiei, or that trichinosis is due to trichinæ must also be regarded as ill-founded.

Cholera.—The etiology of cholera has been attentively studied since the recent outbreak in Egypt, especially by a French Commission under Dr. Straus, and a German Commission under Dr. R. Koch. The former arrived at no definite conclusion; but Koch in his Sixth Report expresses the belief that he has discovered a bacillus which is constantly present in cholera, and which occurs in cholera only. It is distinguished by being more or less curved—comma-like or even semi-circular. It is actively mobile. When cultivated, the bacilli grow into more or less undulating threads of which the terminal cells retain the form of the organisms found in cholera.

These fungi are found only in the intestinal contents and evacuations; when found in vomit, this was shown by its alkalinity to have regurgitated from the intestine.

It is constantly present in very large numbers in rice-water stools, but only in small numbers during the early stage whilst the dejecta are still fæcal, and they rapidly disappear, when recovery occurs, as the motions assume their normal character.

The German Commission believes these bacilli to be the *cause* of the disease, but it seems very doubtful whether this will be at all generally accepted. Unfortunately, all attempts to convey the disease to animals have failed—no animal has ever been known to suffer from cholera.

Malaria.—Klebs and Tommasi-Crudeli* examined the soil, water, and ground-air of malarial districts near Rome. They found in the soil very numerous mobile, long-oval spores (·95 μ in greatest diameter), which on cultivation or on injection into an animal's blood, grow into rods, 60–84 μ long by ·6 μ wide, homogeneous at first, but later dividing transversely. Spores form in the sections, at first parietal, afterwards filling the whole interior. They are aërobious, and grow in albumen and fluids of the body, but not in water. Stagnant water of the district did not contain them. The air did, except during the seasons when malaria was not prevalent; then they are found in the soil only.

Culture-fluid, of which the filtrates had but slight effect, excited in animals typical, regularly intermittent fever with swelling of the spleen, and in severe cases deposit of black pigment in it. Developmental forms of the bacilli were found in the spleen, marrow, lymph, and blood.

Marchiafava† a little later found the same spore-bearing bacilli in the spleen, marrow, blood, and lymph, of patients dead of "perniciosa;" and showed that they were frequently, but not invariably, present in the blood of patients during the *cold* stage of a fit; in the *hot* stage no bacilli were present, but the spores above-mentioned were there in large numbers. Quinine caused the

* *Arch. f. Exp. Path.*, p. 122, vol. xi.
† *Ibid.*, xiii.

disappearance of these bodies. Injection of blood into the trachea and peritoneum of dogs failed to produce the disease. No organisms were present in the remission-stage.

In the blood of a traveller recently returned from Africa, Dr. McMunn found typical B. malariæ during the cold stage.*

Sternberg† failed to isolate the bacillus, and thinks that Klebs produced a septicæmia, not an intermittent fever. He thinks malaria may be due to an organism, but that it has not been found.

Typhoid.—Klebs first described micro-organisms in this disease.‡ He and his assistants found them without exception in twenty-four cases of typhoid—constantly in the bowel and frequently in mesenteric glands, kidneys, spleen, heart, laryngeal cartilages, in patches of lobular pneumonia, and in the pia mater (one case with severe cerebral symptoms). The organism was a short rod which grew into long, narrow, unbranched filaments, of which the diameter increased as spore-formation took place. Klebs cultivated the organism on gelatine, but it is uncertain whether his cultures were pure. He also inoculated rabbits from the cultures, and in one case some swelling of Peyer's patches was found post-mortem.

A few months later, Eberth§ described bacilli, with rounded ends, as existing in the intestinal lesions, mesenteric glands, and spleen. He said that they stained badly with aniline dyes, and worked with unstained specimens clarified by an alkali. He was thus able to discover the bacilli in eighteen out of forty cases. He believed them to be the same as Klebs described, but regarded the filaments, of which the latter author spoke, as secondary. Eberth stated that the number of bacilli diminished with the duration of the case.

* *British Medical Journal*, vol. ii. p. 935, 1881.

† Nat. Board of Health Bull., Washington, 1881.

‡ *Arch. f. Exp. Path.*, vol. xii. p. 231.

§ *Virch. Arch.*, vol. lxxx. p. 58, and vol. lxxxiii. p. 486.

Koch* had already photographed similar bacilli at the time Eberth published. He found that they stained well with Bismarck brown, and had demonstrated their presence in half the cases examined by him.

W. Meyer† took for examination only recently-swollen patches and follicles. He failed to stain the bacilli, but found them in sixteen out of twenty cases.

All the above observers made control observations on other cases, such as tubercular ulceration of the intestine; but they never found the typhoid bacillus in diseases other than typhoid. They sometimes found cocci in the intestine and glands, but regarded them as secondary; but by others, as Letzerich‡ they have been considered as the organism of the disease.

Maragliano§ examined blood from the finger and spleen (during life) of fifteen typhoid patients. During the height of the disease the former contained single and aggregated micro-organisms, almost all spherical, some mobile; in the latter, besides similar bodies, bacilli, like those of Klebs and Eberth, occurred in small number. All disappeared in convalescence. Cultivation of blood from either finger or spleen yielded small rods like those found in fresh blood, and others much longer, like those described by Klebs.

Brautlecht|| has often found a bacillus in epidemics in Brunswick, and has traced it to the drinking water; it forms spores when cultivated. Both bacilli and spores abound in the urine of typhoid patients. Subcutaneous injection of the cultivations in rabbits was followed by high fever, inflammation of Peyer's patches, swelling of the mesenteric glands, and other signs of typhoid. The organism described by Brautlecht is not the same as that of Eberth and Koch, being smaller.

* Mitth. a. d. k. Gesundheitsamte, vol. i. 1881.

† Unters. ü. d. Bacilli d. Abdominaltyphus, Inaug. Diss., Berlin, 1881.

‡ *Arch. f. Exp. Path.*, vol. ix. § *Cbl. f. Med. Wiss.*, p. 725, 1882.

|| *Virch. Arch.*, vol. lxxxiv. p. 80.

Coats and Crooke* have each found the bacilli of Eberth and Koch in mesenteric glands.

A very important paper by Gaffky, one of Koch's assistants, has just appeared.† He starts with the observation that the bacilli have been found in only half the cases examined. They must therefore have either disappeared before the disease which they caused had run its course, or they were present but not found. The latter seemed probable, as they had been demonstrated late in some cases, and missed at early stages in others. He points out that in typhoid the bacilli are not scattered everywhere, but are always in foci, and therefore more difficult to find; and that but little of an organ has been examined, even after 100 sections have been carefully looked through.

Gaffky himself investigated twenty-eight cases, and in twenty-six demonstrated the presence of bacilli in parts other than the intestine—such as the mesenteric glands, spleen, liver, kidney. In the other two cases, the bacilli were found in a recently swollen solitary follicle of one; and the other died at the end of the fourth week of perforative peritonitis, and the intestines showed only healing ulcers.

In one case, which Gaffky does not include in his list, although it had been diagnosed as typhoid, both during life and post-mortem, immense numbers of cocci were found in the organs, and it was impossible to distinguish the typhoid bacilli. Gaffky throws out the suggestion that there may be a disease clinically like typhoid due to invasion of the intestine by cocci.

The bacilli were more numerous the earlier the case. If many are found in old cases, it is probable that a relapse has occurred.

The process employed to demonstrate the bacilli was to harden pieces of *fresh* organs in alcohol, and to place sections cut from them in methylene blue for twenty-four

* *British Medical Journal*, 1882, March 18 and July 1.

† Mitth. a. d. k. Gesundheitsamte, vol. ii., p. 372, 1884.

hours. The solution is made by adding a saturated alcoholic solution of the blue to water until the latter cannot be seen through. The sections are clarified, and mounted in the ordinary way. Blue sections lose their colour rather quickly; those stained with Bismarck brown are better for preservation. It is most important that the organs should be fresh, for the bacilli are difficult to distinguish in sections from putrefactive organisms.

The bacilli are thus described (Fig. 150, 8). They are three times as long as broad, and their length equals one-third the diameter of a red blood corpuscle. Their ends are distinctly rounded. Spores are not uncommonly seen —round, reaching right across the breadth of the rods, and lying at their ends. The typhoid bacilli are more or less actively mobile. They do not stain so intensely as other forms, and sometimes they do not stain uniformly; round spots not extending across the rods, and therefore not spores, being left pale. The typhoid bacilli do not stain like tubercle-bacilli (p. 535).

Thirteen cultures were made from spleens, and eleven were pure from the first; peptonised meat broth stiffened with gelatine being the soil used. It was spread in thin layers upon slides, and these were inoculated in streaks and kept moist under a glass bell. In twenty-four hours increasing cloudiness could be seen confined to the lines, and *not causing liquefaction* of the soil: it was due to roundish, slightly granular, yellow-brown colonies. A little mixed with sterilised water and examined with $\frac{1}{12}$ oil-immersion (Zeiss) showed the colonies to consist of one form of bacillus only; like, but rather larger, than that in the spleen whence culture was started. They were 3-4 times as long as wide; apparently the soil suited them better, so they grew more strongly, as they did also on potatoes; whilst in blood-serum they remained of the same size as in the body. Spores form at the ends of the rods in 3–4 days at 30°–42° C., more slowly at 20° C., and not at all below this point. In smaller number than the rods jointed threads also formed. The cultures reached their

height in 4-8 days, and then remained stationary. The mode of growth in both gelatine and potato was characteristic. Cultivation was continued on the gelatine in ten cases for more than a year without any change occurring in the organism.

In two cases putrefaction had begun in the spleens used, and other organisms, cocci and bacilli, liquefying the gelatine, also grew; but in this solid culture-ground it was so easy to select typhoid bacillus-colonies that the second culture was quite pure.

In one case in which a culture from a spleen succeeded, no bacilli were found in cover-glass specimens, nor in sections until over 100 had been examined. The method of culture would seem to be the most delicate for the detection of the organisms.

A culture from the liver was tried in one case and succeeded.

Many animals of different kinds were inoculated, but unsuccessfully. It is very doubtful if any animal suffers from the typhoid fever of man. In spite of this gap in the chain of evidence, all the observers quoted believe that this bacillus is the cause of typhoid; and we may now say it is constantly present in typhoid, is recognisable from all known bacilli by the various characteristics given above, and is not found in any other disease. Gaffky believes that infection occurs always through the mucous membrane of the intestine; even when the poison seems to have been inhaled as dust, he thinks it sticks on the pharynx, is swallowed, passes through the stomach, and thus reaches the bowel.

At the International Medical Congress in 1881, Bouchard stated that he had found bacilli in the tubules and in inter-tubular tissue in cases of tubal nephritis occurring during typhoid. They have been described by other observers as occurring in the urine.

Septicæmia of Mice.—Koch* injected putrid fluids subcutaneously in mice in quantity too small to cause

* Traum. Infect. Dis., p. 33.

septic intoxication. A peculiar disease, without abscess formation, occurred in some individuals, and was transmissible with certainty to others by inoculation of a very small quantity of blood. Extremely small bacilli, chiefly in leucocytes, were shown to be the cause of the disease. One attack confers immunity. It is not inoculable upon field mice or rabbits.

Malignant Œdema. — A spreading œdema ending fatally may be produced by inoculation of mice, guinea-pigs, or rabbits, with garden-mould. One form of fungus develops, and the œdema-fluid containing it is easily inoculable.

There are two species of the genus **Vibrio**—*V. rugula* and *V. serpens;* they occur in putrefying fluids, and are not pathogenic.

The bacilli of Tubercle, Leprosy and Glanders have already been described.

Order 4.—**SPIROBACTERIA.**—These differ from Vibrio in making more screw-like and closer turns; river-water is their favourite habitat (Cohn). There are two Genera—*Spirochæta*, flexible with wide thread; *Spirillum*, stiff with narrow thread.

Relapsing Fever.—The *Spirochæta Obermeieri* (Fig. 150, 10) often called spirillum, is found in the blood in this disease. It is 16–40 μ long, and makes quick undulating movements. The organisms are generally said to appear in the blood soon after the commencement of an attack, and to disappear with remarkable speed after the crisis. Spitz, however, states* that by careful examination he found spirochætæ in the blood 2–4 hours before and after an attack. Nothing is seen of them till the relapse, when they return. The disease has been inoculated from man on man, and from man on apes (Carter, Koch). Koch cultivated the Spirochæta Obermeieri; it grew into long threads.

Albrecht† took blood from patients after an attack

* Diss., Breslau, 1879.

† *Petersburg. Med. Wochschr.*, 1880, No. 1.

of recurrent fever, kept it in a moist chamber, and examined it frequently. In the first day of the remission he found (1000 diam.) extremely small movable bodies; later these were succeeded by slender rods, each bearing a spore at one end or in the middle; and finally, active spirochætæ appeared after the relapse had begun in the patient from whom the blood was taken.

A spirochæta is often found in carious teeth.

The **Spirilla**—*tenue*, *undula*, and *volutans*—are not pathogenic.

THE BLASTOMYCETES OR YEASTS.

These are small round or oval cells, which multiply by gemmation. Sometimes the cells cohere and form branching chains. When food is not abundant, as when cultivated in potato, turnip, &c., one to four spores may form in the interior of the yeast-cells; these develop when placed in fermentable fluids. Under the same conditions unjointed mycelium may be produced. These facts, taken with the knowledge that some higher fungi (*e.g.*, Mucor Mucedo) under certain circumstances grow as yeasts ordinarily do, by gemmation, make it possible that yeasts are really vegetative forms of higher fungi.

Yeasts are of importance only as causes of fermentation. They never invade living tissues. They are not rare in the stomach, either alone or in company with sarcina. They are frequently found in diabetic urine, but not when it is passed.

Thrush.—In this disease, tolerably adherent grey or milky patches form in the mouth, pharynx, and gullet, either of children at the breast or of adults exhausted by disease (typhoid, phthisis). These patches are due to the growth of the **oidium albicans**, a parasite which was regarded as a mould; but Grawitz states that, when cultivated, this fungus shows itself to be a yeast, and probably the Mycoderma vini, which he has proved capable of growing on mucous membranes. The patches consist of tortuous, often branched filaments, formed of

long cells united end to end, and distinctly constricted where they join. The filaments end in roundish cells, which produce one or more spores; these form heaps in the epithelium.*

THE HYPHOMYCETES OR MOULDS.

These consist of filaments (*Hyphæ*) formed by a single row of cells placed end to end, growing by means of an apical cell which elongates and divides transversely. Lateral offshoots are common, but dichotomous branching is rare. The thallus may consist of a single hypha; usually the hyphæ are numerous, and intercross loosely or closely. All spring from an axis or *germinal tube* which grows directly from a germinating spore. Compared with that of bacteria (p. 483), their growth is extremely slow.

In the adult plant the hyphæ are of two kinds—*nutritive*, which grow into and extract nourishment from the culture-soil, forming in it by their interlacement the *mycelium*; and the *reproductive*, which spring from the mycelium, and stand up from the substance in which the mycelium lies. These are called fruit-hyphæ; they are simple or branched, and bear at their ends spores or sexual organs. Reproduction is either a-sexual or sexual; the two methods may occur together on the same plant, or may alternate regularly or irregularly. Spores are formed by each—round, oval, or cylindrical, smooth or irregular, coloured or colourless; most are motionless, but some "swarm." Each consists of a little mass of protoplasm, surrounded by an envelope, which is made up of an outer (*exosporium*) and an inner (*endosporium*) layer; the exosporium is often pigmented. All spores have great power of resisting the action of physical and chemical agencies, and retain life for long periods; those formed a-sexually are ready at once to germinate, but those due to a sexual process almost always require a

* *Virch. Arch.*, vol. lxx.

rest. The latter are the true *resting-spores;* but this name is often applied to all spores capable of retaining life for long periods in spite of adverse conditions.

To understand the above and what follows, the student should examine a few moulds from the surface of thin jam, paste, decaying fruit, or the surface of a slice of potato which has been exposed for an hour or two in a dwelling-room. In all, the aërial portion is easily studied, and the mycelium is readily shown by crushing a bit of the culture-ground under a cover glass.

A-sexual spore-formation occurs in three ways :—

1. Hyphæ spring from the mycelium, and perhaps branch. The terminal cells divide transversely into spores (*conidia*), which either fall away singly or form chains.

2. A hypha (*sporangiophore*) stands up from the mycelium, and its end swells into a ball full of protoplasm, which segments and forms conidia (*sporangium*).

3. From the surface of a knob on the end of a hypha (*conidiophore*), peg-like processes (*sterigmata*) sprout; each sterigma, by growth and transverse division, forms a chain of spores.

Sexual reproduction occurs in three ways :—

1. **Conjugation.**—The apical cells of two hyphæ meet end to end, and blend into one cell (*zygospore*). From this, after a longer or shorter rest, a sporangiophore sprouts, and from its spores new plants grow. (Any of the Mucorini.)

2. **Fertilisation.**—(*a.*) The end of a hypha becomes twisted like a corkscrew, more and more closely, until its turns form a continuous tube—the *ascogonium*. From its lower turns spring fine branches, one of which (*antheridium*) conjugates by its apex with the ascogonium; the others simply cover the ascogonium continuously, and are converted by division into polygonal cells, which form a capsule (*perithecium*) round it. Many transverse septa form in the tube of the ascogonium, and from the cells thus produced flask-shaped lateral projections (*asci*) develop; in each of these eight spores generally appear. The

perithecium thins greatly as the asci enlarge, the walls of the asci disappear, and an easily ruptured sphere of spores remains. When these germinate the endospore swells, splits the exospore, and puts out the germinal tube, whence springs the mycelium. This again gives origin first to conidiophores, then to perithecia. Eurotium repens, and Aspergillus glaucus, found especially on preserved fruit, show these changes.*

(*b*) In some species certain cells form an organ—*oogonium*—in which female reproductive bodies—*oospheres*—one or more, are formed; whilst other cells form a male organ—*antheridium*—in which *spermatozoids* are produced. The oosphere, which is hundreds of times larger than the spermatozoids, remains in the oogonium, and is there fertilised by the mobile spermatozoids. It is now called an *oospore*, and may, after a rest, develop directly into a new plant, or form cells, each of which does so.†

Conditions of Life.—Food.—Possessed of no chlorophyll, moulds are unable to build up carbon-compounds; they assimilate those built up by other plants or animals. They are therefore always either saprophytes or parasites; in the latter case they may kill their host. They require a free supply of oxygen; but some can obtain it, at least for a time, by decomposition of organic compounds like sugar. Thus, Mucor racemosus, cultivated on the surface of a saccharine liquid, absorbs oxygen, oxidises completely some of the sugar, exhales carbonic acid, and grows rapidly. If deprived of oxygen, as by immersion, only the mycelium grows, and this becomes broken up into short cells, which multiply by budding, and much resemble yeast-cells. The growth is much slower, carbonic acid escapes in bubbles, and alcohol appears in the liquid. But soon all stops, and the process can be started again only by a fresh supply of

* Sachs, Text-book of Botany, p. 257.
† *Ibid.*, p. 212.

oxygen.* Some moulds, as Penicillium glaucum, Aspergillus niger, have no power of thus obtaining oxygen, and die if cut off from the free gas. The change in the character of growth above-mentioned, accompanying change in conditions of life, is often pointed to as evidence in favour of the mutability of bacteria.

Light.—Many moulds can develop completely without it: some require it for the discharge of spores and other processes.

Temperature.—Ziegler states that moulds flourish best at temperatures below that of the body (37·5°), and that some will not grow at this point. A few species of Aspergillus and Mucor grow well between 35° and 40°. The spores are as resistant to external agencies as are those of bacteria.

Water is essential, but mere dampness is sufficient.

Action.—Moulds are associated with processes of *rotting* or *decay*. The peculiar smell and taste which they impart is known to all. The products of their life-action have not been closely investigated; but they are neither very poisonous nor irritant to man.

Distribution.—The spores of moulds are much more numerous in the air than are other organisms. They, therefore, constantly fall upon the skin and enter the air-passages with air, and the food passages with food. As a rule, they find no nidus suitable for their development; the supply of free oxygen is often insufficient, and the temperature too high. Certain of them, however, when brought into contact with accumulated inflammatory discharges, or with sloughs, take root and fructify. This is most likely to occur in the respiratory tract, and the alimentary tract above the gullet. They are here saprophytes, but the products to which they give rise may irritate the living tissues lying beneath the soil in which they grow. Species of Mucor and Aspergillus are thoes commonly found.

* Duclaux, p. 5.

Pathogenic Moulds.—Owing to the peculiarities mentioned in their life-history, these fungi have but little power of invading living tissues. Certain skin-diseases are, however, due to the growth of species of this class in epidermic structures: they are—Favus; tinea tonsurans, kerion, circinata, sycosis, and unguium; and tinea versicolor. Two diseases, actinomycosis, and the Madura foot of India, have been attributed to penetration of the deeper tissues by hyphomycetous fungi.

Favus.—The *Achorion Schonleinii* forms almost wholly the light, yellow, mouldy-smelling crusts, characteristic of **Favus.** When in hairy parts, which are the usual seats, the hairs are always invaded, especially the roots. Here, the parasite grows luxuriantly, but it does not extend far up the shaft; its primary seat is the epithelium of the hair-follicle. On non-hairy parts the mycelium invades the deeper layers of the epidermis. The mycelium consists of unjointed, branching, confusedly intercrossing tubes; in certain of them, which become divided into joints, oval spores form.

The nails are very rarely affected, and chiefly by mycelium.

The *Trichophyton tonsurans* is the cause of tinea tonsurans, tinea kerion, tinea circinata, tinea sycosis, and tinea unguium.

In **Tinea tonsurans** the hair is chiefly affected; the root and the lower part of the shaft are crammed with spores which lie in rows between the fibrils of the hair. The weakened hair breaks beyond the scalp, leaving a stubbly line of fracture. Epidermic scales from the surface may contain fungus, but the deeper living cells of the root-sheath never. (Thin and Taylor.) Spores are abundant, and oval in shape; mycelial threads are rare. Points worth remembering in relation with the undoubted fungoid origin of the disease, are its occurrence in children only (speaking broadly), the predisposition to it shown by some, its great contagiousness when acute, diminishing as it becomes chronic, and its more severe course when con-

tracted from animals, as the horse. It may excite severe irritation and even suppuration—*T. kerion.*

Tinea circinata.—Here the parasite infests epidermic cells, always causing desquamation, sometimes vesiculation, or even more severe inflammation. Mycelium chiefly is present in the form of very long, jointed and branched threads; the spores are scanty, single, or in short chains. The fungus altogether is often scanty, and is especially difficult to detect if it has excited inflammation.

Tinea sycosis.—When attacking the beard the fungus is found chiefly in the hair, but also in the follicle; both mycelium and spores are seen, the latter in excess, but not so markedly as in T. tonsurans. The mycelium generally lies round the root of the hair, and is pulled out of the sheath with it. Severe inflammation is generally excited.

Tinea unguium.—Mycelial threads of trichophyton may occasionally invade a finger-nail, rendering it opaque, thick and brittle. Unlike a general condition, the fungus produces these changes in 1–3 nails only, and the toe-nails are scarcely ever affected. In this situation it is extremely difficult to destroy.

Chloasma, Pityriasis versicolor.—*Microsporon furfur* invades the horny layer of the epidermis of covered parts of the trunk, growing more superficially than any of the above, rarely causing irritation and not attacking nails or hair. It consists of jointed mycelial threads which are always abundant; and spores, which vary much in form, and grow at the ends of the mycelial threads.

Actinomycosis.—The ray-fungus (*actinomyces*) is believed to be the cause of this disease. It has been described at p. 329. Its botanical position is doubtful.

Madura Foot.—In certain parts of India the feet of natives, only, swell; tubercles form beneath the skin, burst, and leave sinuses from which bodies like those constituting the roe of a fish are discharged, or, more rarely, bodies like grains of gunpowder. In the former, fungi have never been found; but in the latter, after soaking for some days in potash, fungous elements have

been recognised and called, *Chionyphe Carteri*. These are believed by some (V. Carter) to be the cause of both classes of the disease. Cunningham and Lewis do not hold this view (Quain's Dictionary). On section, masses of the above bodies are seen, especially in the fatty layer; the masses may have no obvious communication with each other, or with the surface. The botanical position of the fungi found is doubtful.

METHODS OF DEMONSTRATING THE PRESENCE OF PATHOGENIC MICRO-ORGANISMS.

These vary according as they are used for the investigation of (*a*) fluids or (*b*) tissues.

(*a*) **MICRO-ORGANISMS IN FLUIDS.**—1. Simple microscopic examination may be sufficient to reveal organisms of distinctive form or possessing marked powers of locomotion. No preparation will be necessary beyond mounting a thin layer of blood or other fluid.

2. Recklinghausen pointed out the resisting power of many of these organisms to alkalies and dilute acids: solutions of these were formerly used to clear away fatty and albuminoid particles, but nowadays they are employed only as a part of complex staining processes.

3. **Staining.**—This is by far the most important method, and it is to Weigert that we owe the introduction of the reagents—the aniline dyes. Logwood stains many fungi well, but it has no preference for them over animal tissues, so it does not cause them to stand out. The aniline dyes most often used are gentian violet, methyl violet, and methylene blue, or Bismarck brown for photography; watery solutions are employed, from ½ to 5 per cent. Cover-glasses and slides should be cleaned in very dilute nitric acid and kept in alcohol; before use they should be heated in a spirit flame whilst held in forceps. Take two cover-glasses which have just cooled, place a *small* drop of

the fluid on one, put the other glass on the top of it, squeeze the glasses gently together, and then glide one off the other, so as to leave a *very thin* layer of the fluid on each. Now dry both cover-glasses by passing them several times through a spirit flame. A temperature of 120° should be reached for a few minutes to produce insolubility and fixation to the glass of any albumen. If a weak staining solution is used, the glasses must be floated on it for some time; but a strong solution (2–5 per cent.) is quite as good, and stains deeply in less than a minute. Pour a little on to the glass, pour it off after a few seconds and wash with distilled water from a wash-bottle; dry over a flame. Warm a slide, and just melt on it a little solid balsam; drop the slightly warmed cover-glass on to this and press it down.

For fluids rich in albumen a concentrated solution of aniline brown in glycerine and water (equal parts) may be used with advantage.

Certain organisms are distinguished by holding to basic aniline dyes, as fuchsine, gentian violet, methyl violet, &c., which they have taken up slowly from fluids which may be either alkaline or acid (Ziehl), when they are acted on by a solution of nitric acid (1 in 3), whilst everything else is decolorised—including other kinds of bacteria. These latter and the tissues may, after the acid has been washed off, be stained with some contrast-colour—*e.g.*, fuchsine and methylene blue. This method will be described under "tissues." The chief fungi known to stain in this way are B. tuberculosis and B. lepræ; a coccus also has been met with. B. tuberculosis is now constantly sought for in pus, in sputum, and in urine for purposes of diagnosis, or to learn the result of treatment.

For the examination of fluids for B. tuberculosis, Gibbes' double stain is the quickest, and is said to be as reliable as any (Vignal).

(*b.*) **MICRO-ORGANISMS IN TISSUES.**—Tissues for examination should be placed as soon as possible after death in methylated spirit. When thoroughly hardened,

very thin sections must be cut either by hand or by some microtome. If a freezing machine is used, a thinnish slice of the tissue must be soaked in plenty of water for two or three hours, and then put into mucilage (B.P.) for a similar time. The sections are to be placed for two hours or longer in a one per cent. watery solution of the dye selected; warmth facilitates staining. Some workers transfer the stained section to a one per cent. solution of glacial acetic acid, then to absolute alcohol, and finally to oil of cloves: others put them straight into alcohol. Each one of these fluids dissolves the dye out of the tissue, and the difficulty is to carry the sections through them rapidly enough. It is best, therefore, at first to take only one section at a time out of the staining fluid. One or two trials will show how long the section must be left in each fluid in order that it may still retain a rather pale colour when it is spread out on the slide. Superfluous oil of cloves is now run off, and the section dried with a piece of clean filter-paper pressed firmly on it. A drop of Canada balsam dissolved in xylol is put on the cover-glass, and this is applied; chloroform- and benzol-balsam slowly dissolve out the stain, and pure balsam is rather difficult to work with.

If a blue or violet stain has been used, the sections, after washing in alcohol, may be dipped in water for a moment and then placed in eosine- or carmine-solution for an hour; the tissue-elements acquire a red tint, whilst the organisms remain blue or violet. The sections must now be carried through alcohol and oil of cloves; then mounted.

To examine tissues for B. tuberculosis or B. lepræ, Ehrlich's process is the best. Many contrast stains may be used; we shall speak of fuchsine and methylene blue. To 100 c.c. of water add 4 c.c. of pure aniline (ordinary aniline is much cheaper and very good), shake well and filter; to the filtrate add 11 c.c. of a saturated alcoholic solution of fuchsine. Prepare also a saturated solution in absolute alcohol of methylene blue; and dilute nitric acid (B.P.)

with two parts of water, or with three, if this decolourises too quickly. Place the sections in the fuchsine solution for at least two hours in a warm place; then transfer them to the nitric acid solution and leave them until the colour is almost gone; then rinse them in water, and put them into methylene blue for an hour. Now pass them through absolute alcohol and oil of cloves, and mount as above. Either B. tuberculosis or leprae will appear red on a blue ground; all other organisms present will be blue.

With large and delicate sections it is a good plan to use the glass slide as a section lifter, pushing it obliquely into the cloves or even the alcohol, and there spreading the section out upon it. Large vessels and plenty of the fluid must be used for this purpose.

With large organisms or with successful contrast-staining a power of 500 diams. and ordinary illumination will be sufficient for most purposes; but for the smaller fungi the highest powers made, and a sub-stage condenser of very wide angular aperture, are necessary.*

CULTIVATION.—Having determined the presence of organisms in a fluid or tissue, it may be wished to cultivate them, to study their life conditions or to inoculate the pure organisms on other animals.

Three methods may be mentioned—cultivation in fluids, in solids, and in living animals.

In Fluids.—Klebs introduced a method which he called "Fractionirte Cultur." It consists in adding to a sterile fluid a small quantity of a fluid or substance containing the fungus. Under suitable conditions the latter will grow. A small quantity of the culture-fluid may then be added to another flask, and so on until all vestiges of what was inoculated in the first flask along with the original organisms must have disappeared. If more than one kind of fungus is inoculated, or if in the inoculation of successive flasks contamination from the air or apparatus

* Koch. Transm. Inf. Dis. p. 97

occurs, it may be impossible to obtain a pure cultivation of one organism.

In Solids.—Koch, therefore, introduced a solid culture-ground. Clear meat-broths and other fluids are peptonised and have added to them sufficient gelatine (2½–3 per cent.) to render them solid at 20°–25° C., at which temperature most fungi will grow fairly. Klein, however, finds it necessary for the latter temperature to have at least 10 per cent. of gelatine present. A thin layer of the gelatine may be spread on a cover-glass; a recently-heated wire, having on it the material to be examined, is drawn across the gelatine in two or three lines, and the cover is inverted over a glass cell. Examination will now show what organisms are present, and where the one it is wished to grow is situate; the growth may be watched, and fresh culture-grounds inoculated from it. As the inoculation takes place in air, organisms may fall upon the gelatine, or the wire may catch one or two. The latter would lie in the inoculation-lines, the former would probably be away from them, and therefore at once recognisable. Examination of several lines guards against the former fallacy. A very handy method of cultivation is the inoculation of slices of recently boiled potato, made with a pure knife, and kept under a bell-jar in moist air. Most frequently such cultivations are carried on in test-tubes. For methods of preparing these and inoculating them, see Klein.*

In Animals.—Koch injected fluids containing many kinds of organisms into the bodies of animals. In only one case did two organisms develop, and then whilst one (bacillus) was in the blood, the other (coccus) remained in tissues round the inoculation-puncture. The former gave rise to septicæmia, and could be easily inoculated alone; but the latter, which caused spreading gangrene, could not be obtained free from the bacillus until both were inoculated on an animal, in which the latter could not grow, whilst the former flourished. Pure cultivation of each could now

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PRINTED BY BALLANTYNE, HANSON AND CO.
LONDON AND EDINBURGH