Aids to pathology.

AIDS
TO
PATHOLOGY

HARRY CAMPBELL

SECOND EDITION

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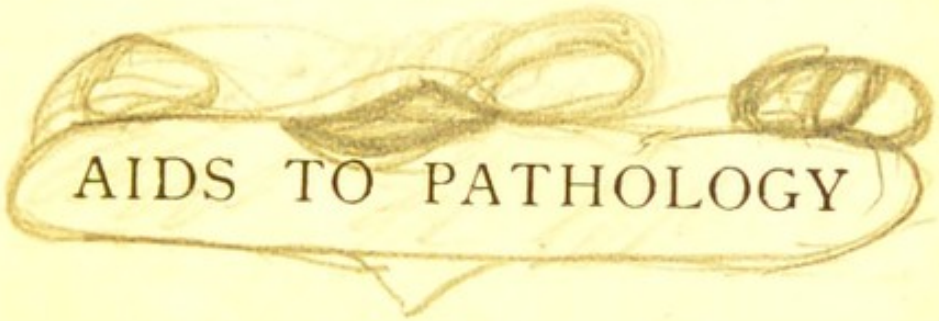
CInf^n – Result of inflamm^n process
being able to destroy infecting matter

Sep^s

Pyaemia – Pus in blood – form
/ Pyogenic organism circul^n in blood & sep^n out to
or small abscess (numerous) form^n in body

Streptococcus viridans causes
ulcerative endocarditis


AIDS TO PATHOLOGY

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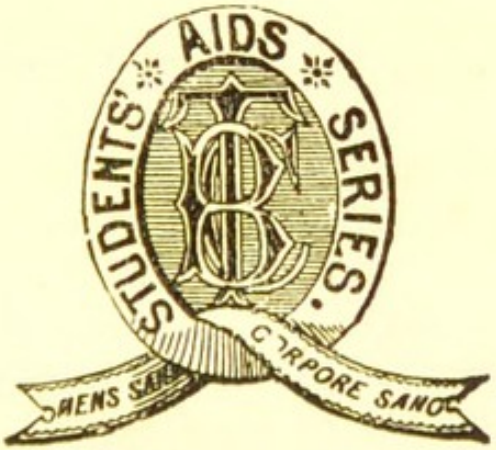
SECOND EDITION



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PREFACE TO SECOND EDITION

THIS edition has been carefully revised and brought up to date. A chapter on Diseases of the Heart has been added, many other chapters have been expanded, and some entirely rewritten. As the subject of Immunity looms large on the pathological horizon, the chapter dealing with it has been considerably amplified, and the latest views on the subject embodied in it. An effort has been made to state clearly the rationale of the Wassermann reaction.

H. C.

LONDON,
December, 1910.

PREFACE TO FIRST EDITION

I HAVE endeavoured in the following pages to present concisely, and as briefly as possible, the known facts of Pathology.

There is no pretence to a complete or exhaustive treatment of the subject. The student must regard the description of each disease as a framework into which he can fit all the information acquired from the post-mortem room, the museum, and the laboratory.

It is hoped that the section on 'Immunity and Opsonins' may help to elucidate a somewhat difficult problem in serum-therapeutics.

H. C.

November, 1907.

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AIDS TO PATHOLOGY

'Every illness, every intoxication, has caused the formation, perhaps the destruction, of a certain substance in the blood, and has left its natural trace, a trace which is not effaced by years. Just as there is the psychological memory, facts which are present to the consciousness, so there is a humoral memory of all preceding infections. As these infections differ in each person in intensity, quantity, and duration, it follows that each person differs from every other in the chemical properties of his blood.'—PROFESSOR CHARLES RICHET.

THE BRICKS OF THE BODY.

The Cell.—The organic unit is the cell: it bears the same relation to the body that the brick does to the house. It consists of cytoplasm (*cytos* = the cell), composed of a contractile, reticulated framework, the *spongioplasm*, soaked in a nutrient lymph, the *hyaloplasm*.

In typical cases, the cytoplasm is surrounded by a cell-wall, and contains a nucleus and nucleoli. The cell lies bathed in lymph, which, though at times tending to stagnate locally, as in the muscles during rest, may be regarded as more or less continually on the flux, flowing both through and around it. The *lymph-flow* to the cell carries the oxygen, proteins, carbohydrates, fats, salts, and other substances necessary for the biochemical changes that constitute cell life; the *lymph-ebb* carries away from the cell the waste-products, such as carbonic acid and ammonia.

The *nucleus*, the most highly specialized part of the cytoplasm, constitutes, as it were, the inner 'cabinet' of the cell, presiding over and inspiring its many activities. It is motile, shifting its position in the cytoplasm from time to time. Like the cell itself, the nucleus is bounded

by a membrane, the nuclear wall, which is achromatic (*i.e.*, no affinity for basic dyes—*chroma* = colour), and contains the nuclear *spongioplasm* and a fluid—the *nuclear hyaloplasm*, or karyolymph.

The nuclear spongioplasm is achromatic, but imbedded in it are small granules, called *chromatin granules* (consisting of nuclein) from their great affinity for basic dyes. At the points where the threads of the spongioplasm

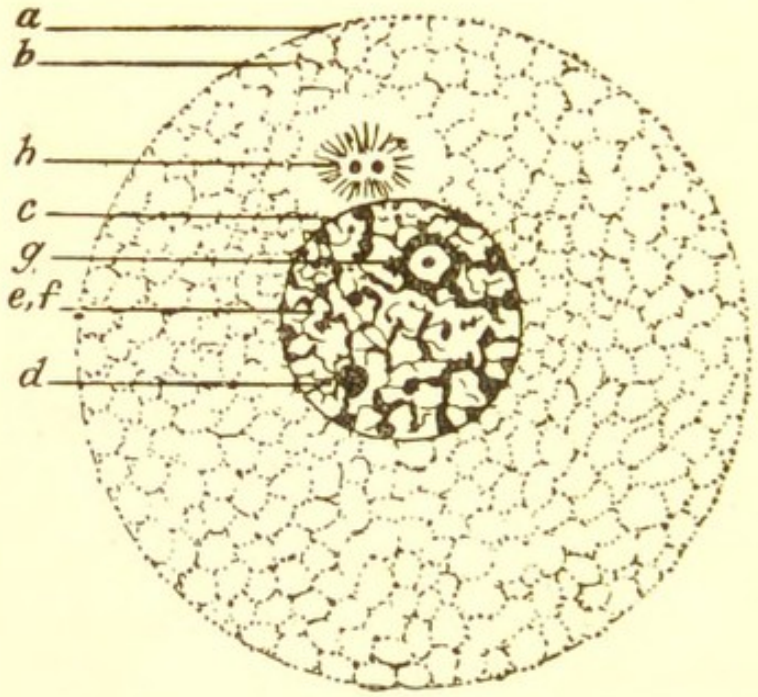

FIG. 1.

Cell wall; *b*, spongioplasm, enclosing the hyaloplasm; *c*, nuclear wall; *d*, karyosome; *e*, *f*, nuclear spongioplasm, enclosing the nuclear hyaloplasm; *g*, nucleolus or plasmosome; *h*, astral system, with divided centrosome.

intersect the chromatin granules may be heaped up into larger masses, called *karyosomes*.

The *nucleolus*, or plasmosome, contained within the nucleus, is usually single, but there may be as many as five nuclei. It is oxyphil (*i.e.*, stains with acid dyes). In its interior is a minute body—the *endonucleus*—the function of which is unknown.

The *centrosome* lies in the cell cytoplasm, just outside the nucleus. Usually there are two centrosomes placed side by side, enclosed within a membrane, from

the exterior of which radiate delicate fibrils—the *astral system* of the centrosome.

The centrosome appears to be connected with cell reproduction, initiating, as it does, the process in mitotic division.

Cell Division.—The nucleus, the dynamic centre of the cell, divides. This division may be :

1. *Direct*, *simple*, or *amitotic*. The nucleus becomes constricted at its middle, and then by simple fission separates into two parts The cell cytoplasm now divides, each half carrying a nucleus. The result is the production of two cells.

2. *Indirect* or *mitotic*. The chromatin granules collect into threads (*mitos* = a thread), which subsequently undergo a complex series of changes (known as karyokinesis) prior to the ultimate division of the cell into two parts.

Mitotic division is the rule, amitotic division is the exception—it is said to occur in malignant tumours.

Note.—Oxyphil, eosinophil } = affinity for acid dyes.
Basophil = affinity for basic dyes.
Amphophil = affinity for both.
Neutrophil = no affinity for either.

Cell Disease.

The structure of the various cells of the body depends primarily upon the constitution of the zygote (= fertilized ovum) which gives origin to them. Their behaviour during life depends upon their structure as thus hereditarily determined, and upon the influences brought to bear upon them from without. These influences are *plasmic* and *non-plasmic*.

Non-Plasmic Influences.—These consist for the most part of nerve stimuli, which, originating in sensory end-organs, either on the surface, or in the deeper tissues, of the body, are continually reverberating throughout the entire nervous system, and thus influencing not only individual neurones, but non-nervous cells (such as muscle cells and gland cells) attached to the ends of efferent nerve fibres. If we reflect that the human organism con-

sists essentially of a nervous system from the ends of whose efferent nerve twigs so many muscle and gland cells depend, the whole being held together by connective tissue, and permeated by a complex system of channels for the circulation of the body-fluids, and that nerve stimuli are ceaselessly reverberating throughout the nervous system, we shall the better realize how potently that system must influence the individual cells of the body.

Plasmic Influences.—These operate through the lymph bathing the cells, and depend upon the composition of that lymph, which, again, is essentially determined by the composition of the blood plasma. This is a highly complex fluid —the most complex in nature, containing an endless variety of substances—food-stuffs, oxygen, hormones, ferments, opsonins — most of which defy the most careful and delicate methods of chemical research; and let the fact ever be remembered that it is in a fluid of this kind that, from the beginning to the end of its career, every cell in the body lies bathed, and is through it subjected to an endless variety of influences, both good and bad.

Now, the cells of the body display little or no intrinsic tendency to disease: *the cell environment, notably the plasmic environment, is chiefly responsible for whatever disease may affect the cell.* Even senile cell degeneration is largely extrinsic in nature, for though doubtless it is in part intrinsic—due to the running-down or wearing-out of the cell microcosm—it is even more the result of specific changes in the plasmic environment of the cell. Senility is, in fact, mainly of plasmic origin, the individual being slowly destroyed by means of his plasma—not, indeed, by any such simple and pathological process as that suggested by Metchnikoff—*i.e.*, by the absorption of bacterial toxins from the large intestine—but by the operation of complex physiological mechanisms, the object of which is to put a definite term to the vital cycle, and thus to obviate the innate tendency to immortality belonging to all living matter. In some animals—*e.g.*, the dog—these mechanisms come into operation sooner than in others—*e.g.*, man. Sometimes in man they come into premature operation, the arteries becoming sclerosed, the skin

wrinkled, and the hair grey as early, it may be, as the second decade; at others their operation is delayed, the nonogenarian being as youthful, it may be, as the average man of fifty or sixty.

If we except cases of intrinsic senile degeneration, it but very seldom happens that a cell *primarily becomes diseased.* The nearest approach to such a phenomenon is afforded by the family palsies, in which definite systems of neurones undergo early degeneration.

Hence, in every case of cell disease we should suspect the existence of some morbid influence operating on the cell from without. This influence may be *nervous* or *plasmic.*

Cell Disease from Nervous Causes. — A familiar instance is the degeneration which takes place in the striped muscle fibre when its motor twig is diseased. All the instances of genuine *trophic lesions* are due to some interference with the normal flow of nerve impulses into the cells 'trophically' damaged.

Degeneration from Plasmic Causes.—Much the most common cause of disease of the cell is some abnormality in respect of the plasma bathing it. Abnormalities of this kind fall under two heads:

1. *Defects in the Circulation of the Plasma.*—These may be central, as in heart and lung disease; or local, as in embolism, and degeneration of the smaller blood-vessels.

Any sudden and pronounced interference with the local circulation leads to profound degenerative changes, as in infarct (see p. 65). More chronic defects of the circulation, as in chronic heart disease and senile degeneration of the arteries, lead to gradual atrophy of the parenchyma cells and increase of the fibrous elements. In the former case the sluggish circulation causes damage of the capillary walls, with escape of the chromocytes into the tissues and subsequent staining of the tissues from their disintegration, as illustrated in the well-known 'nutmeg liver.' In the latter case the fibrous change may be termed *senile fibrosis*, and is chiefly responsible for the toughening of the tissues observed in old age.

2. *Defects in the Composition of the Plasma.*—The composition of the plasma may depart from the normal in

an untold number of ways. Thus the plasma may vary in respect of its nutrient constituents, its ferments, its hormones, and its normal waste products. Furthermore, it may be poisoned (*a*) as the result of morbid metabolism, as in diabetes; (*b*) by the introduction of a poison such as lead or alcohol, into the body; and (*c*) by bacterial and other parasitic toxins formed within the body.

The vast majority of non-traumatic diseases result from the action of a morbid plasma upon the tissue cells How wide is the rôle which the plasma plays in disease is evident from the fact that a toxic state of the plasma is the sole cause of inflammation; and how largely this process bulks among the diseases which the physician is called upon to treat is evident from a casual perusal of any textbook on medicine.

But morbid plasma induces many lesions other than the inflammatory. Thus the blood may contain substances which exert a noxious action, chiefly or entirely, upon certain kinds of cells, picking them out, as we say, by selective action, much as the pigments used for staining microscopic sections pick out some cells rather than others. A familiar instance of this is afforded by tabes dorsalis. This disease is a sequela of syphilis, and is due to the action of a poison which causes degeneration in certain sensory neurones; and it is probable that most of the 'system lesions' of the nervous system—*i.e.*, symmetrical lesions of particular tracts—have a similarly plasmic origin.

In such cases the degenerative changes are for the most part chronic. Morbid plasma may, however, set up acute destructive changes in special kinds of cells. Experiments have shown that the tissues of animals, such as the dog and the rabbit, can be made to elaborate substances capable of causing rapid destruction of special cell types, such as chromocytes, hepatic cells, and renal cells; and there can be little doubt that substances of this kind play an important part in disease. Thus, acute yellow atrophy of the liver is produced by the action of some toxin which is to all intents and purposes a hepatolysin (see p. 38), and certain forms of 'acute pancreatitis' probably own a similar pathology.

VARIETIES OF DEGENERATION.

Strictly speaking, *degeneration* is simply the reverse of evolution; it is an undoing, so to speak, of evolution. Thus, when the dendrites of a neurone diminish in number, as they do in old age, or when the transverse striæ of a muscle disappear, degeneration takes place.

The pathologist, however, often uses the term 'degeneration' in the chemical rather than in the structural sense. For him it often means the conversion of the complex protoplasm into some new and much simpler substance, such as fat or colloidal material.

As already stated (p. 4) cell degeneration is rarely spontaneous, but almost always due to some morbid influence operating on the cell. Such morbid influences operate, above all, through the plasma.

To trace out the various degenerative changes which may be produced in the tissues by morbid conditions of the plasma would be impossible, even did space permit. *When we reflect that each abnormality of the plasma must tend to produce its own particular change in the tissues which that plasma bathes, it is obvious that the degenerations which protoplasm undergoes must be far more numerous than those as yet described by pathologists.*

Degeneration must be distinguished from **infiltration**—*i.e.*, the deposition of some new substance in an otherwise unaltered cell.

Some of the more common forms of infiltration and degeneration will now be considered.

Infiltrations.	*Degenerations.*
Glycogenic infiltration.	Cloudy swelling.
Fatty infiltration.	Chromatolysis.
Calcification.	Fatty degeneration.
	Amyloid degeneration.
	Hyaline degeneration.
	Mucoid degeneration.
	Colloid degeneration.

Glycogenic Infiltration.

Glycogen is normally present in the liver, in embryonic tissues, and, indeed, to some extent in most cells. *As a*

morbid process, infiltration of glycogen occurs in malignant tumours, and in the leucocytes in cases of suppuration, pneumonia, and other acute infections.

The test for glycogen is the mahogany-brown colour it gives with iodine (the iodide of glycogen).

Fatty Infiltration.

In fatty infiltration tiny globules of fat appear in the cell, *the protoplasm of which, however, remains healthy.* The globules may coalesce and push the protoplasm against the cell wall. Fatty infiltration is the normal condition of many connective tissues (*e.g.*, of the medulla of the long bones) and, to a less extent, of the liver. *It is only when the number of fat globules exceeds the normal limit that the term 'fatty infiltration' is applicable.*

The causes are excessive diet, especially if coupled with insufficient exercise, and alcoholism, particularly beer-drinking. Excessive deposit of fat may also occur from an anabolic habit of body, as in the monstrously fat people seen in shows, and in myxœdema. In all such cases the cause is probably a peculiar condition of blood, in consequence of which the fat is not properly metabolized. 'Adiposa dolorosa' is a condition in which a nodular deposit of fat is associated with considerable superficial pain.

An excessive local deposit of fat may result from disuse, as in the case of the muscles of a fractured limb which has been put up in splints.

Calcification.

Calcification is the deposition of lime salts (phosphate and carbonate) in degenerated or dead tissues.

According to Klotz, a necessary preliminary to calcification is the formation of *soaps* in the degenerated or dead tissues.

Sites.—Arteries, especially the aorta and coronary (very rarely the veins), valves of the heart, old tubercular lesions, certain tumours (*e.g.*, fibro-myomata of the uterus), the capsule enclosing the *Trichina spiralis*, adherent pericardium, the walls of old abscesses, the fœtus of an ectopic

gestation (forming lithopædion or peritoneal calculus), the thyroid, costal, and other cartilages in old people.

Cloudy Swelling.

In cloudy swelling the cells become swollen, their cytoplasm 'cloudy' from the presence of fine granules, and their nuclei obscured. The granules, which are probably albuminous in nature, are dissolved by acetic acid and alkalies, but, unlike fat, are insoluble in ether and do not stain black with osmic acid. If the degeneration has not advanced too far, the cloudiness may clear up and the cell resume its normal appearance, but if it continues to advance it may pass into fatty degeneration.

Cloudy swelling occurs in connection with febrile states (pneumonia, diphtheria, scarlatina, enteric, etc.). It is produced by the action of bacterial toxins, its distribution being determined by the nature of the toxin, the organs most frequently affected being the kidney, liver, and heart.

Chromatolysis.

One of the first signs of degenerative change in the neurone is the absorption of the stainable Nissl granules (chromatolysis). The change begins in the neighbourhood of the nucleus. The granules are first converted into fine dust, and ultimately disappear.

Fatty Degeneration.

In fatty degeneration the cell protoplasm is replaced by fat, the fat being split off from the protoplasm molecule. The fat first appears as minute, highly refractile granules, which gradually increase in number until, it may be, the whole cell is converted into a mass of fat. The fatty contents stain black with osmic acid, and reddish-orange with Sudan III., and dissolve in alcohol and ether, but not in acetic acid.

Fatty degeneration is typically found: In severe and prolonged anæmias—*e.g.*, fatty degeneration of the heart always occurs in pernicious anæmia; from the action of certain poisons, notably alcohol, chloroform, iodoform, phosphorus, and arsenic; from the action of certain bacterial toxins—*e.g.*, pneumonia, diphtheria, enteric,

tuberculosis. *Heart*, *liver*, and *kidneys*, are the organs principally affected.

Waxy, Lardaceous, Amyloid, or Degeneration.

This is a condition in which peculiar changes occur in the cytoplasm of certain *connective tissues*, whereby they become homogeneous, translucent, and 'waxy.' The change involves more especially the connective tissue of the middle and inner coats of the arterioles, and the sub-endothelial layers of the capillaries. The endothelium itself is never affected, nor are parenchyma cells of any sort (muscle, gland, nerve).

The disease is met with most frequently in the kidneys, spleen, and liver. The lungs and central nervous system are exempt from it.

In 118 cases examined post mortem by Dickinson the frequency in which the various organs were affected was as follows:

Kidney	95	Lymph glands ...	5
Spleen	76	Pancreas	1
Liver	65	Thyroid	1
Intestines	35	Œsophagus	1
Stomach	9	Testes	1
Suprarenals ...	9	Endocardium ...	1

The waxy material stains a deep mahogany-brown with iodine, turning blue or violet if 5 per cent. sulphuric acid is afterwards applied. With methyl violet it gives a deep rose-pink (normal tissues are stained blue).

This degeneration is found in connection with chronic suppuration, particularly that due to tuberculosis. It also occurs in syphilis, both acquired and congenital.

The waxy material is of the nature of a *gluco-protein*. It is not a precipitate from the blood or lymph, but in all probability results from the action of bacterial or cellular toxins, for the organs most affected (kidneys, spleen, liver, and intestines) are those most concerned in the elimination and neutralization of toxins.

In the Liver.—The organ is greatly enlarged, smooth, firm, and heavy, with its edges rounded. The cut surface is pale, translucent, and wax-like. The change *commences in the subendothelial layer of the capillaries of the intermediate zone of the liver lobule* (see Diseases of

the Liver), the lining endothelial cells of the capillaries remaining unaffected. The pressure of the new material upon the liver cells causes them to become fatty and to undergo atrophy.

In the Kidneys.—These organs become pale and enlarged, and the capsule strips off readily. The cut section has a translucent, bacon-like appearance. The change begins *in the vessels of the glomerular tufts and in the arteriæ rectæ.* Later on, the basement membrane of the tubules (especially of the cortex) may suffer. The lining epithelium of the tubules tends to undergo fatty degeneration, owing to interference with the circulation.

In the Spleen.—There are two varieties of lardaceous spleen:

The *sago-spleen*, commonest in phthisis. In this the organ is but slightly enlarged. On section it is seen studded with small, translucent, sago-like bodies, which vary in size from a millet-seed to a hemp-seed, and give the ordinary amyloid reactions. The change begins in the arterioles and capillaries of the Malpighian bodies.

The *diffuse waxy spleen*, commonest in syphilis. The organ is greatly enlarged, and becomes hard and firm. On section it shows a uniform translucent appearance. The walls of the sinuses of the splenic pulp specially exhibit the change.

Hyaline Degeneration.

Hyaline degeneration (*hyalus*, glass) occurs in the subendothelial lining of the intima of the smaller arteries, particularly of the spleen, kidneys, brain, spinal cord, and to a lesser extent, the lymphatic glands. The change is also to be found in tubercles prior to caseation, and in tumours. On section the material looks glassy and shining. With picro-carmine it stains at first pink; later on, yellow.

The degeneration occurs in connection with certain acute infections, notably diphtheria and scarlatina, and is therefore probably caused by the action of toxins. It is of a protein nature, and closely allied to amyloid, mucoid, and colloid material. Some authorities consider it to be but a preliminary stage of lardaceous disease.

Mucoid Degeneration.

The gluco-protein *mucin* is a normal secretion of the mucous membranes, and is poured out in increased quantity when they become inflamed. It is met with as part of a degenerative process in chondromata, sarcomata, carcinomata, and other tumours. The affected cells and fibres swell up, and become transformed into a jelly-like substance.

In water the mucin swells up; it is soluble in dilute alkalies, from which it is precipitated both by alcohol and acetic acid.

In ovarian cysts an allied substance—*pseudomucin*—is found. This differs from mucin in not being precipitated by acetic acid.

Colloid Degeneration.

Colloid (*kolla*, glue) is a normal constituent of the thyroid gland and the pituitary body, being derived from *epithelium*, the cells of which become detached and glued together into a solid mass. As a degeneration, it is most frequently met with in cancers of the abdomen, especially of the stomach, intestine, ovary, and peritoneum. It also occurs in cancer of the breast, and in congenital cystic disease of the kidney.

The material resembles mucin in appearance, but is insoluble in water, and is not precipitated by alcohol, nor by acetic acid.

PIGMENTATION.

'Pigmentation' (*pingo*, paint) is the term used to denote an abnormal deposit of colouring matter in the tissues. The pigment usually lies *within the cells* of the pigmented area.

Melanin.—This is the most common normal pigment of the body. It contains nitrogen, hydrogen, and carbon, and often sulphur; also iron, at the early stage of its formation, but later on it becomes iron-free. It is bleached by chlorine, a feature which distinguishes it from carbon. It is not a product of the disintegration of hæmoglobin, but it is elaborated by cell action from an albuminous substance, and is normally present in the skin, hair, iris,

choroid, and cardiac muscle. The quantity of it in the skin is augmented by solar rays, at the climacteric in women, and often during pregnancy ; also in leucoderma, Addison's disease, Graves' disease, granular kidney, rheumatoid arthritis. Melanin constitutes the pigment met with in melanotic sarcoma ; in certain cases of this disease it may be found in the urine (melanuria).

Lipochromes. — These are pigmented fats containing melanin, and are normally found in the corpus luteum. Pathologically, they are present in xanthoma and chloroma. It is not yet decided whether the pigment in brown atrophy of the heart is due to ordinary melanin or to the presence of lipochromes. (Lipochromes are also found normally in certain ganglion cells, and sometimes in degenerated nerve cells).

The *hæmatogenous pigments* are derived from the breaking up of the chromocytes.

The hæmoglobin molecule is very complex. It is represented approximately by $C_{758}H_{1203}N_{195}O_{218}FeS_3$ (Mann). When of no further use, the chromocytes are broken down in the liver, spleen, bone-marrow, and kidneys, the residual pigment being decomposed into (*a*) the iron containing *hæmosiderin*, which is used in the manufacture of new chromocytes, and (*b*) the iron-free *hæmatoidin*, which is chiefly excreted as a waste product by the liver in the form of bilirubin.

Hæmosiderin, or *iron-containing* pigment, is found in those diseases (*e.g.*, pernicious anæmia and malaria) in which there is a pathological destruction of the chromocytes. In pernicious anæmia large quantities may be found, in the form of minute granules, in the cells of the intermediate zone of the liver lobules, as well as in the spleen, renal epithelium, and bone-marrow. In the kidneys it may be present in a diffuse form.

Hæmatoidin, or *iron-free* pigment, is generally derived from extravasated blood, the hæmoglobin being first converted into hæmatin and then into hæmatoidin. It is often seen in the remains of old blood-clots in the form both of *granules* and orange-coloured rhombic *crystals*, which may remain unaltered for years.

According to Neumann, living cells are necessary for the elaboration of hæmosiderin, but not of hæmatoidin.

Pigmentation from Bile.—Jaundice is now thought to be *always* due to some form of obstruction to the outflow of bile from the liver, and to its subsequent absorption into the circulation, by which it is carried throughout the body. The pigmentation is the result of a *diffuse staining* of the tissues with bilirubin and biliverdin, and is specially marked in the conjunctiva, the skin, and beneath the tongue. (The toxic effects of jaundice are probably referable to the bile-salts.)

Extrinsic pigments are those introduced into the body from without. The chief examples are—

Through the lungs	Carbon, coal, iron, or grit, deposited in the lungs and bronchial glands.
Through the alimentary tract	Arsenic, silver, deposited in the skin.
Through the skin:	Tattooing.

NECROSIS.

The term 'necrosis' (*necrōsis*, deadness) signifies death of a portion of the bodily tissues. If it is preceded by degeneration of the cells of the affected part, it is sometimes called *necrobiosis*.

The principal forms of necrosis are: focal necrosis, fat necrosis, coagulation necrosis, and caseation.

Focal Necrosis.—In this condition numerous minute areas of tissue—generally in the *liver*, *spleen*, *kidneys*, or *lymph glands*—undergo a focal necrosis. The protoplasm of the part disintegrates, the cell walls disappear, and a granular substance replaces the original tissue. The necrotic foci may be either absorbed or converted into fibrous tissue.

The most probable cause is a toxin, which may act directly by killing the cells outright, or indirectly by causing capillary thrombosis. It occurs in enteric fever, diphtheria, and probably in most of the other microbic infections.

Fat Necrosis.—This is a condition in which localized patches of necrosis are found in the fatty connective tissues of the abdomen. In a large majority of cases it is associated with pancreatic disease (*e.g.*, hæmorrhage, abscess, gangrene). It is supposed that the fat-splitting

ferment (steapsin) of the pancreatic juice escapes, and acts directly upon the parts affected. It is met with typically in the *subperitoneal fat*, in the omentum, mesentery, and under surface of the diaphragm, being most marked in the immediate neighbourhood of the pancreas, and often occurring in that organ itself. In these structures are to be seen, scattered throughout the normal fat, small opaque foci, ranging in size from a pin's head to a pea. The fat of the affected areas is converted into a granular material which does not stain with osmic acid.

Coagulation Necrosis.—This generally occurs in connection with inflammation, and is probably always toxic in origin. It is typically seen in diphtheria. In this disease the mucous membrane is acutely inflamed: the epithelial cells of the affected part, bathed in inflammatory lymph, are killed outright by the bacillary toxin; coagulation, both of the cell-contents and of the surrounding lymph, then takes place, and the two fuse into a homogeneous hyaline mass, which in course of time assumes a grey colour.

Zenker's Degeneration is now regarded as a form of coagulation necrosis. It affects muscle fibres: these swell and lose their transverse striation, while the muscle-proteins coagulate into a clear homogeneous material, which soon breaks up into shiny masses of irregular shape. Zenker's degeneration is met with in continued fevers, notably enteric, and is chiefly met with in the abdominal muscles.

Caseation (*caseus*, cheese).—This is a post-necrotic change in which the cells disintegrate, lose their outline and nuclei, and are converted into a yellow, homogeneous, cheesy mass, composed of fatty and albuminous granules. It is most often met with in tubercular and gummatous formations and in certain rapidly growing tumours, and is due in part to the cutting off of the blood-supply by thrombosis, and in part to toxic action.

ATROPHY.

By atrophy is meant an abnormal decrease in the size alone, or in both the size and number, of the elements of

a normally developed tissue. The condition has to be distinguished from *hypoplasia*, in which there is defective development.

Atrophy is generally associated with a certain amount of fatty degeneration. It affects essentially the *parenchyma* of an organ (*e.g.*, muscle fibres, gland cells, nerve cells), the connective-tissue stroma, as a rule, escaping. The stroma, indeed, increases whenever the parenchyma atrophies.

Physiological atrophy, such as occurs in the thymus, in the uterus after parturition, in the ovaries after the menopause, is known as *involution*.

The protoplasm of an atrophying cell becomes unwontedly clear, staining less than normally, and the nucleus disappears. Often there is increased pigmentation—a phenomenon well seen in brown atrophy of the senile heart.

Atrophy may be general or local.

Causes of General Atrophy.—General wasting of the tissues may be caused either by :—

Decreased anabolism, the result of impoverishment of the blood, such as occurs in starvation, and cancer of the œsophagus, and stomach ; or by

Increased katabolism, such as occurs in severe fevers, tuberculosis, congenital syphilis. In these cases the general wasting is chiefly to be ascribed to the action of toxins in augmenting katabolism. The wasting which occurs in Graves' disease and from the administration of thyroid extract is also due to heightened katabolism, the thyroid (or parathyroid) yielding to the blood some substance which plays the part of a vital bellows, causing the vital fire to blaze, as it were.

The Causes of Local Atrophy are :—

Lessened Functional Activity—e.g., atrophy of the muscles of an arm or leg encased in splints.

Excessive Functional Activity.—Usually this is preceded by hypertrophy. Examples are : the sterno-mastoids and other cervical muscles in emphysema and the biceps brachialis in file-grinders.

Pressure—e.g., atrophy of the bodies of the vertebræ or sternum owing to the pressure exerted by an aneurism ;

atrophy of the liver cells caused by the pressure of the fibrous tissue in alcoholic cirrhosis.

Defective Neuro-trophic Influence—e.g., facial hemi-atrophy. We are still in the dark as to the pathology of this curious affection, but it is probably nervous in origin. The changes which take place in the muscles in consequence of disease of the lower motor neurones are rather of the nature of degeneration than atrophy,

Diminished Blood-Supply—e.g., atrophy of the testis caused by pressure on the spermatic artery by a tumour. Here, again, the changes are degenerative rather than simply atrophic.

Hypertrophy.

By hypertrophy is meant an abnormal increase in the *size* of the tissue elements. If the tissue elements increase in number the term *hyperplasia* is employed. As a rule, hypertrophy and hyperplasia go hand in hand.

True hypertrophy must be distinguished from pseudo-hypertrophy. In the former there is hypertrophy principally of the parenchyma; in the latter, of the connective tissue only. Thus, in pseudo-hypertrophic paralysis some of the muscles may appear to be enormously enlarged, but the enlargement is brought about by the increase of fatty and fibrous elements, the muscle fibres themselves having largely disappeared.

The usual cause of hypertrophy is increased functional use, which is always accompanied by increased blood-supply. Familiar examples are hypertrophy of the heart in valvular disease, of one kidney when the other is removed, of one leg when the other is crippled or paralyzed. Muscular hypertrophy, if excessive, is liable to be followed by atrophy.

In some cases hypertrophy is due to the influence of an internal secretion. Substances of this kind which are capable of exciting the functional activity, or the growth, of a tissue are termed by Starling *hormones*. Secretin, which is formed during duodenal digestion, and, passing into the blood and circulating through the pancreas, excites the secretion of this organ, is an instance of the effect of a hormone in influencing functional activity; a substance yielded by the fœtus, which causes the mammæ

to develop in the pregnant female, is an example of a hormone which is capable of exciting growth.

Normal growth is largely controlled by hormones, which are poured out at definite periods (infancy, childhood, puberty), and determine the developmental changes incidental to these periods. If these hormones are not duly secreted, development may be arrested at any one of them, giving rise to infantilism, arrested puberty, and allied conditions. On the other hand, if they are formed in excess, or are perverted, they may lead to hypertrophy: both acromegaly and gigantism are to be explained in this way.

THE BLOOD AND ITS DISEASES.

The blood consists of a fluid—the plasma—in which float the blood-corpuscles.

The *plasma* contains, besides its waste products, nutrient proteins, carbohydrates, fats, and salts, as well as a multiplicity of other less-understood substances necessary to normal nutrition, such as hormones and ferments. It is continually oozing through the thin walls of the capillaries to replenish the lymph.

The *lymph*, which is a *dilute* plasma, is the medium of exchange between the blood and the tissues, conveying to these latter food and oxygen, and carrying off their waste products. It provides the cells of the body with a saline medium reminiscent of that inhabited by their far-off amœboid ocean ancestors.

The blood-corpuscles are of three kinds:

The coloured, called *chromocytes* (or erythrocytes);
The *blood-platelets*;
The colourless, called *leucocytes*.

The Chromocytes (Erythrocytes).

The chromocytes of all mammals in health are non-nucleated (except in embryonic life and immediately after birth). Although authorities differ, the general consensus of opinion is that in health their numbers approximately are 5,000,000 per cubic millimetre in man, 4,500,000 per cubic millimetre in woman. Their average diameter is

7·5 μ ($\frac{1}{3200}$ inch), and in health does not vary more than 1 μ in extent. (The Greek letter μ = a micromillimetre = $\frac{1}{1000}$ part of a millimetre = $\frac{1}{25000}$ inch). Their shape in all mammals (except the camel) is that of a biconcave disc. This shape is due to the fact that the original spherical body collapses with the disappearance of the nucleus. Their average duration of life is about three weeks.

Such influences as food, pregnancy, and lactation have but slight influence on their number during health, but living in high altitudes may cause an increase. An augmentation to the extent of 2,000,000 per cubic millimetre has been observed at a height of 6,000 feet above the sea-level. A similar increase has been observed in the cyanosis of congenital heart disease and in mitral stenosis.

Source.—The nucleated red cells (normoblasts) of the bone-marrow, the nucleus being extruded.

Blood-platelets.—These are discoid bodies, measuring about a quarter of the diameter of the red blood cell. According to some authorities they are simply the escaped nuclei of the normoblasts. They appear to initiate the process of thrombus-formation, and compose the chief mass of the vegetations in endocarditis. They number about 250,000 per cubic millimetre.

Abnormal Chromocytes.

Non-nucleated	Microcytes.
	Megalocytes.
	Gigantocytes.
	Poikilocytes.
Nucleated, or erythroblasts	Normoblasts.
	Megaloblasts.
	Gigantoblasts.
	Microblasts.

Microcytes (or small chromocytes) vary in diameter from 3 μ to 6 μ. They are found in most forms of anæmia.

Megalocytes (or large chromocytes) vary in diameter from 8 μ to 16 μ. They are typically met with in pernicious anæmia, but they may be present in any kind of severe anæmia.

Gigantocytes.—These are enlarged forms of megalocytes. They may exceed 20 μ in diameter.

Poikilocytes (oval, pear-shaped, or fiddle-shaped chromocytes) are present in many varieties of anæmia.

Erythroblasts (or nucleated chromocytes) only display their nuclei when stained. Nucleated red blood cells are present during intra-uterine life, but are never seen in healthy blood after birth, except for the first few days of life. They are found especially in pernicious anæmia, but they may occur in any severe kind of anæmia. They are of four varieties, according to their size :

Normoblasts, of the same size as the normal chromocytes. These are normal to the red marrow, and normally pass into the blood minus their nuclei. The nucleus is rendered conspicuous by nuclear stains. They are often abundant in pernicious anæmia.

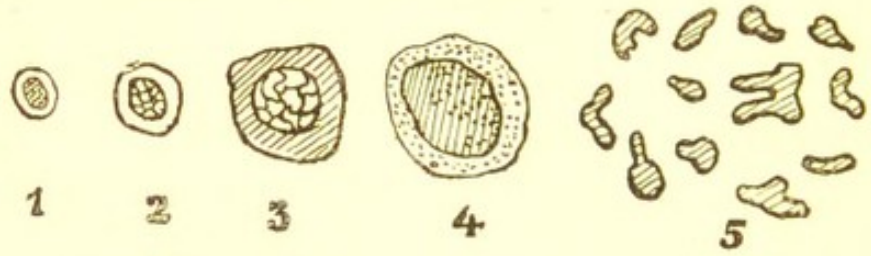

FIG. 2.—ABNORMAL BLOOD CELLS (DIAGRAMMATIC).

1, Microblast ; 2, normoblast ; 3, megaloblast ; 4, myelocyte ; 5, poikilocytes.

Megaloblasts, of greater size, and even double that of the normal chromocytes (10 μ to 16 μ in diameter). The nucleus, which may occupy two-thirds of the cell, stains faintly with the nuclear dyes. Megaloblasts occur in pernicious anæmia, and in the anæmia of *Ankylostomum duodenale* and of *Dibothriocephalus latus*.

Gigantoblasts.—These resemble the preceding, but are larger, sometimes exceeding 20 μ in diameter.

Microblasts, which are the small nucleated chromocytes. They are found in all forms of anæmia, and are of but little diagnostic importance.

Colour-Index—Estimate of the Amount of Hæmoglobin.

Decrease in the number of the chromocytes, and decrease in the amount of hæmoglobin in the blood, do

not necessarily go hand-in-hand. The severity of most anæmias is better estimated by the deficiency of hæmoglobin than by the number of chromocytes; in chlorosis, for example, the number of chromocytes may be but little, if at all, diminished, while the amount of hæmoglobin in each individual chromocyte may be much reduced.

The amount of hæmoglobin (Hb) in each individual chromocyte (C) is called the colour-index. It is the ratio of the hæmoglobin percentage to the corpuscle percentage.

The colour index is obtained by means of the formula

$$\frac{o/c\ \text{Hb}}{o/c\ \text{C}}.$$

Percentage of Chromocytes.	Percentage of Hæmoglobin.	Colour-Index.
In health - 100	100	$\frac{100}{100}$, or 1
In chlorosis - 60	30	$\frac{30}{60}$, or 0·5
In pernicious anæmia - 20	30	$\frac{30}{20}$, or 1·5

Leucocytes.

In fœtal life the leucocytes make their appearance later than the chromocytes.

In normal blood the proportion of leucocytes averages 8,000 per cubic millimetre, their ratio to the chromocytes being thus as 1 to 600 or 700.

In health the following kinds of leucocytes are found:

The small lymphocytes =22 to 25 per cent.
The large lymphocytes = 2 to 4 per cent.
The polymorphonuclears=70 to 72 per cent.
The eosinophiles = 2 to 4 per cent.
Mast cells = 0·5 per cent.

—Ehrlich.

The *small lymphocyte*, 6 μ to 8 μ in diameter. It contains a large, spherical, deeply-staining nucleus, which occupies almost the entire cell. It is non-amœboid and non-phagocytic, and constitutes 22 to 25 per cent. of the total leucocytes. *Source:* All lymphoid tissue.

The *large lymphocyte*, also termed hyaline (the macrophage of Metchnikoff), 9 μ to 15 μ in diameter. Its nucleus stains less intensely than that of the small lymphocyte. It is amœboid and phagocytic, and constitutes from 2 to 4 per cent. of the total leucocytes; in malaria this variety is usually abundant. *Source:* The small lymphocyte.

Transitional forms between (1) and (2).

The *polymorphonuclear*, also termed neutrophile (the microphage of Metchnikoff), 9 μ to 12 μ in diameter. The nucleus stains deeply, and may assume, as its name implies, a variety of different shapes, such as a lobulated or horseshoe-shape, or it may be twisted like the letters S or *Z*. It is both amœboid and phagocytic, and by far the most numerous of all the leucocytes, constituting

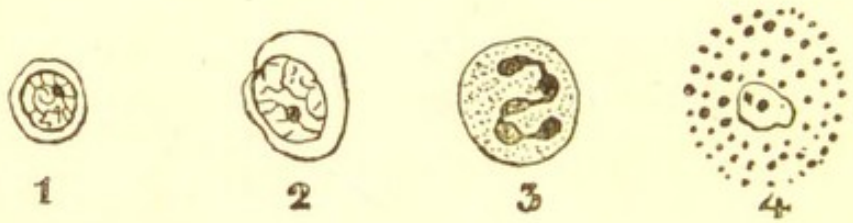

FIG. 3.—NORMAL LEUCOCYTES (DIAGRAMMATIC).

1, Small lymphocyte; 2, large lymphocyte; 3, polymorphonuclear; 4, eosinophile.

from 70 to 72 per cent. of the total. In most bacterial infections it undergoes a great increase in number. Pus cells consist almost entirely of the polymorphonuclear leucocytes. In leucocytosis they generally form the preponderating element. *Source:* Bone-marrow.

The *eosinophile*, 10 μ in diameter, so called because the large, coarse, refractile granules which it contains stain readily with eosin. The nucleus stains faintly with the basic dyes. It is amœboid, but probably not phagocytic, and constitutes from 2 to 4 per cent. of the total leucocytes; in certain diseases due to animal parasites it may be much more numerous. *Source:* Bone-marrow.

The *mast cell* (basophile), 20 μ in diameter, and containing irregular nuclei, which stain feebly. The protoplasm resembles that of the eosinophile in containing coarse

basophile granules. It constitutes about 0·5 per cent. of the total leucocytes; the only disease in which it shows an increase is spleno-medullary leukæmia. *Source:* Bone-marrow.

Myelocytes, or Marrow Cells.—Myelocytes are the parent cells of the polymorphonuclears normally found in bone-marrow, but are never present in healthy blood. They measure from 10 μ to 20 μ in diameter, and have a large but feebly staining nucleus. They differ from the large lymphocytes in containing a fine granular protoplasm. They are numerous in the blood in spleno-medullary leukæmia, in which they may constitute from 30 to 60 per cent. of the total number of leucocytes, and are also found in the blood in pneumonia, smallpox, in fatal cases of diphtheria, sarcoma of bone, and osteomyelitis.

Bone-Marrow.

In infancy and childhood bone-marrow is composed of a tissue resembling the splenic pulp, the **red** or **lymphoid** marrow. By the age of puberty the red marrow in the shafts of long bones has been largely converted into fat—the **yellow** or **fatty** marrow—that in the epiphyses, the flat and the short bones, still remaining red. In old age the fat is to a considerable extent replaced by fibrous and gelatinous tissue, and the same result may be brought about by debilitating diseases.

Functions.—Bone-marrow is the manufactory and storehouse for all the red blood cells, and most of the white. If there is an urgent call for more chromocytes, there is an 'erythroblastic' response; if the call is for more leucocytes, there is a 'leucoblastic' response. Phagocytic—*i.e.*, for pneumococci, streptococci, staphylococci, etc.

Leucocytosis.

By this term is meant an increase in the total number of leucocytes in the blood. Any number over 10,000 per cubic millimetre may be regarded as constituting leucocytosis, so long as the increase lasts sufficiently long. (A physiological leucocytosis occurs from three to four hours after every meal, when the leucocytes may reach from 10,000 to 12,000 per cubic millimetre, but this soon passes off.) It may also occur after the administration of certain drugs—*e.g.*, salicylates, chlorate of potassium, and phenacetin, as also after giving thyroid extract, bone-marrow,

and nucleic acid. It has been observed after operations. Leucocytosis is natural in pregnancy and childhood (lymphocytosis), just before death, and after exercise and massage.

The presence or absence of leucocytosis may be of material aid in forming a differential diagnosis, as, for example, between pleural effusion and empyema, a leucocytosis reaching to 20,000 per cubic millimetre being indicative of the latter; again, a leucocytosis of 20,000 per cubic millimetre has led to the detection of an hepatic abscess or a pyosalpinx as against the diagnosis of enteric fever.

Leucocytosis may assume either (*a*) a *general* or (*b*) a *single type.*

(*a*) *General leucocytosis* occurs in all the general infectious diseases except enteric, measles, German measles, Malta fever, malaria, mumps, influenza, miliary tuberculosis, when unaccompanied by a mixed infection (= aleucocytosis). The leucocytosis in all these cases begins early and increases until the disease has reached its full development. It also occurs in certain cases of malignant growths, and after hæmorrhages.

(*b*) *Single-type leucocytosis:*

(i.) Polymorphonuclears	All local inflammations, especially when accompanied by suppuration; pneumonia; the incubation period of the specific fevers, except those in which there is aleucocytosis.
(ii.) Small lymphocytes	Lymphatic leukæmia, rickets, scurvy, hæmophilia, syphilis, whooping-cough, lympho-sarcoma, certain infantile diarrhœas.
(iii.) Large lymphocytes	This form suggests a protozoon disease, such as malaria, trypanosomiasis, kala azar.
(iv.) Eosinophiles	Asthma, emphysema, eczema, urticaria, psoriasis, lupus, pemphigus, trichinosis, ankylostomiasis, *Bilharzia hæmatobia*, gout, uræmia, myelogenous leukæmia.

The Purpose of Leucocytosis.

The essential purpose of leucocytosis is to aid the resistance of the body against bacterial invasion by increasing the number of phagocytes. It is evident that in some way the bone-marrow (and in the case of lymphocytosis, the lymphoid tissues) is stimulated to increased leucoblastic activity, and, accordingly, we must postulate that the infecting bacteria give off a substance which, passing to the bone-marrow, induces there an augmented production of leucocytes (see Chemotaxis, p. 43).

Leucopenia.

In this condition there is a decrease in the number of leucocytes. It occurs in pernicious anæmia, in very severe anæmias, in splenic anæmia, in the early stages of enteric, in pneumonia—if alcoholic or fatal—and in kala azar.

Anæmia.

By anæmia is meant that condition in which there is a deficiency in certain constituents of the blood; it is a comprehensive term, and embraces three conditions:

Oligæmia = a decrease in the total quantity of blood.
Oligocythæmia = a decrease in the number of chromocytes.
Oligochromæmia = a decrease in the amount of hæmoglobin.

These may occur separately or together.

(The normal chromocytes, born in the red marrow of bone, live for a few weeks only, and then die of senile decay.)

It is obvious that an anæmia may result either from *interference with hæmogenesis*, *i.e.*, defective blood formation—or from *hæmolysis*, *i.e.*, excessive blood destruction. These two factors often co-operate.

Chlorosis.

Chlorosis is probably due to defective blood formation, and affects young women, chiefly between the ages of fourteen and twenty-four. Want of fresh air and sun-

light, deficient exercise, unsuitable feeding occurring at the most critical epoch in a woman's life (puberty and early womanhood), appear to be the most important contributory causes. It has been suggested that the actual cause is an infection causing an inadequacy of the chromocyte-forming elements of the bone-marrow, the infection possibly coming from the alimentary tube. Von Noorden attributes the disease to some abnormality in the internal secretion of the ovary.

Blood Changes.—The specific gravity of the plasma is unaltered. The outstanding feature of the disease is that the hæmoglobin-index is less than 1—*i.e.*, the amount of hæmoglobin in the individual chromocyte is below the normal standard, and may fall even to 20 per cent. of the normal.

The plasma is increased in amount, *the volume of blood being greater than in health.* Although the number of chromocytes per cubic millimetre is generally reduced (sometimes to as few as 2,000,000), their entire number must be increased, because, as Lorrain Smith has shown, the total quantity of hæmoglobin in the blood is normal in amount.

Microcytes and poikilocytes are often present, and in severe cases megalocytes, normoblasts, and even megaloblasts.

The leucocytes are unchanged, and there is no leucocytosis.

Complications.—Œdema, venous thrombosis, fatty degeneration, visceral inflammations, optic neuritis.

Pernicious Anæmia.

Pernicious anæmia is probably due to excessive blood destruction. This conclusion is arrived at from the fact that there is a deposition of an iron-containing pigment —a product of disintegrated hæmoglobin—in the liver, spleen, kidneys, and bone-marrow.

The cause is uuknown ; it is probably a hæmolytic toxin, perhaps developed in the alimentary tract. Very similar blood changes may occur in connection with *Ankylostomum duodenale*, *Dibothriocephalus latus*, gastric cancer, and malaria.

Blood Changes.—These changes are of the nature of a reversion to the embryonal type of blood. Specific gravity is lower than normal; the total quantity of the blood is lessened, and its coagulability reduced. The *chromocytes* are much reduced in number; when the case first comes under observation they may number only 2,000,000, and towards the end may sink to 500,000, per cubic millimetre. In a case of Quincke's they were only 143,000 per cubic millimetre. The number, however, often oscillates within wide limits. Under treatment periods of temporary improvement may occur.

Relatively, the hæmoglobin is increased, so that the hæmoglobin index is greater than 1, and may reach 1·8.

Microcytes, poikilocytes, megalocytes, megaloblasts, gigantocytes, and gigantoblasts, are plentiful. The nucleated red cells may appear suddenly (= blood crisis).

It will be observed that so far as regards the variety of red blood cells, the blood tends to revert to the embryonic type.

Leucocytes.—As a rule there is leucopenia (especially of the polymorphonuclears), the number of leucocytes in some cases being as low as 1,000 per cubic millimetre.

Hæmosiderin (or iron-containing pigment) is found in the liver, spleen, and kidneys (hydrochloric acid + ferrocyanide of potassium = Prussian blue).

Bloodvessels.—There is a great tendency to hæmorrhages in the skin, retina, brain, uterus, and serous membranes.

Bone-Marrow.—The yellow marrow of the long bones reverts to the megaloblastic fœtal type—*i.e.*, is transformed into a red lymphoid tissue, suggesting red-currant jelly in appearance, and containing a large number of red nucleated cells and megaloblasts. The myelocytes are diminished in number. The yellow marrow largely disappears, and much of the surrounding bone is absorbed.

Heart.—Fatty degeneration always occurs. 'Thrush-breast' markings are usually to be seen on the interior of the ventricles.

Liver.—Usually enlarged from fatty degeneration. If the cut surface be treated with ferrocyanide of potassium, and afterwards with hydrochloric acid, the lobules become mapped out by rings of Prussian blue, owing to

the presence of free iron (hæmosiderin) in the peripheral and middle zones.

Spleen.—Occasionally shows the presence of hæmosiderin.

Kidneys.—Usually show fatty degeneration (especially of the convoluted tubules) and the presence of hæmosiderin.

The *gastro-intestinal* mucous membrane usually shows atrophy.

Nervous System.—Sclerosis of the posterior columns of the cord may be present.

Splenic Anæmia (or Primary Splenomegaly).

This very chronic disease is characterized by a great enlargement of the spleen, and progressive anæmia of the chlorotic type, and leucopenia. There is a tendency to hæmatemesis, melæna, and epistaxis. The lymphatic glands are not enlarged.

The chromocytes are diminished in number, frequently falling to 2,500,000 per cubic millimetre, and occasionally to a smaller number. The leucocytes may fall to 800 per cubic millimetre.

The hæmoglobin index is considerably below the normal.

The enlargement of the spleen is uniform, and may be considerable; there is great increase of the stroma, and the Malpighian bodies are atrophied and transformed into fibrous tissue.

Banti's Disease.

This is probably an advanced form of splenic anæmia, being a combination of splenic anæmia with definite cirrhosis of the liver, causing jaundice and ascites. Hæmorrhages from the skin and mucous membranes are common.

Leukæmia (Leucocythæmia).

Leukæmia is a disease characterized by an enormous and persistent increase in the number of leucocytes as the result of pathological changes in the spleen, bone-marrow, or lymphatic glands, or in any two or in all three of these. The actual cause is unknown; it is probably an infection, and of a different kind in each variety. Hughes Bennett,

in 1845, first drew attention to it, describing his case as one of 'suppuration of the blood.' Later in the same year Virchow recorded a similar case, and gave the disease its present name (*leukos*, white, and *haima*, blood).

Two chief forms are recognized—the 'spleno-medullary' and the 'lymphatic,' and there are probably many intermediate forms; in fact, cases have been recorded where the 'spleno-medullary' has turned into 'lymphatic' form, and *vice versa*.

Spleno-Medullary (or Myelogenous) Leukæmia.

This affection takes its name from the fact that it is associated with marked changes in the spleen and bone-marrow. It runs a course lasting from two to five years, and is probably due to an infection.

The *spleen* increases enormously, and may weigh 18 pounds. It is often adherent to the surrounding viscera. On section it is pale, the splenic pulp and fibrous stroma are seen to be greatly increased, and the Malpighian bodies are indistinct. It contains an abundance of myelocytes, mast-cells, and polymorphonuclears. Numerous yellowish necrotic areas of infarctions (probably thrombotic) may be seen in its substance.

The *bone-marrow* is hypertrophied and highly vascular; and, owing to the enormous numbers of myelocytes present, it presents a creamy appearance.

The *blood* is sometimes merely pale, at others it looks like a mixture of blood and pus, and in extreme cases it resembles pure pus. The specific gravity is generally subnormal.

The *leucocytes* are enormously increased, and, in marked cases, may reach from 100,000 to 650,000 per cubic millimetre; but this number is liable to fluctuate from time to time.

Very characteristic is the presence of *myelocytes* (marrow cells), which generally constitute from 30 to 60 per cent. of all the leucocytes present.

The *eosinophiles* are usually increased in number, and the *chromocytes* diminished. *Nucleated chromocytes* (erythroblasts) are a constant feature at some stage or

other of the disease. As already stated, it is the only disease in which the *mast-cells* show an increase.

Charcot-Leyden crystals are sometimes found in the blood after its removal from the body. They are octahedral in shape, and are probably a crystalloid product of either the plasma or the leucocytes.

Hæmorrhages, especially from mucous membranes, are common.

Lymphatic Leukæmia.

This form of leukæmia is associated with enlargement of the lymphatic glands throughout the body. These may attain the size of walnuts. The spleen is also generally enlarged, though only moderately. This variety is much rarer than the spleno-medullary, and runs a more acute course. Like the latter it is probably due to an infection.

The *leucocytes* are increased in number, but not to the same extent as in spleno-medullary leukæmia, their numbers varying between 50,000 and 700,000 per cubic millimetre. The increase is due almost entirely to the presence of *lymphocytes*, which may constitute from 95 to 98 per cent. of all forms of leucocytes present.

There are two types of the disease :

The *large lymphocyte* type (= acute cases and in children).

The *small lymphocyte* type (= the common form, observed in chronic cases and in adults).

The *chromocytes* are nearly always decreased in number.

Acute Leukæmia.

This is a very rare disease, and runs a fatal course within a few weeks or months. It may be either of the spleno-medullary or lymphatic type; more commonly it is of the latter. The leucocytosis rarely exceeds 100,000 per cubic millimetre, the increase affecting principally the small lymphocytes. The chromocytes are usually diminished in number.

Hodgkin's Disease (Lymphadenoma, Lympho-Sarcoma, Pseudo-Leukæmia).

This disease is characterized by an enlargement of the lymphatic glands throughout the body, with which is usually associated an increase of the lymphoid tissue in

the tonsils, pharynx, and intestines, also the development of lymphoid nodules of about the size of peas in the spleen (*hard-bake* spleen), liver, and kidneys. It generally starts in a single group of glands (most often the cervical or axillary), and gradually implicates the other groups.

The Blood.—At the commencement of the disease the blood is normal; later on, anæmia of the chlorotic type may appear. There is no leucocytosis, except that towards the end there may be a moderate increase of the polymorphonuclears.

This negative character of the blood is of value in differentiating the disease from leukæmia.

Chloroma.

This is a very rare disease. According to Byrom Bramwell, it is distinguished by the following characters:

The presence of lymphoid growths in the orbits, temporal fossæ, and periosteum of the cranial bones; the greenish colour of these growths; the studding of the bone-marrow, spleen, lymphatic glands, and viscera with lymphoid deposits; an enormous increase of the lymphocytes. The growths resemble lymphosarcomata in structure (*vide* p. 91).

INFLAMMATION.

By the term 'inflammation' is connoted the succession of phenomena occurring in living tissues as the result of toxic irritation, the irritant toxins being for the most part bacterial in origin. It is essentially an antitoxic and bactericidal process, and, far from being a wholly morbid process, is, in point of fact, Nature's carefully-planned and cunningly-executed fight against disease; it is, in short, a defensive mechanism. Cases of inflammation resulting from the action of non-bacterial toxins—*e.g.*, gouty arthritis, the pericarditis of Bright's disease—are comparatively rare, and may, perhaps, be explained on the supposition that the organism mistakes, as it were, a non-bacterial poison for a bacterial one. Such agents as heat, electricity, Röntgen rays, mechanical irritation, initiate inflammation probably by facilitating the play of toxic forces, especially of those produced by the innumerable microbes which always lie buried between the cells of the epidermis.

Seeing that bacteria play such a dominating part in setting up inflammation, anything which diminishes the bactericidal power of the body necessarily predisposes to it. It is in this way that states of so-called 'lowered vitality,' such as may result from privation, fatigue, chronic alcoholism, Bright's disease, promote the process (*vide* Immunity).

Phenomena of Inflammation.

1. *Dilatation* of the vessels in the inflamed area (sometimes preceded by an initial constriction of the arterioles), with *acceleration* of the blood-stream.
2. *Retardation* of the blood-stream, with accumulation of the leucocytes along the walls of the bloodvessels, the endothelial cells of which swell up.
3. *Active migration* of the polymorphonuclears, especially into the surrounding tissues. Metchnikoff regards this as the essential feature of all inflammations. Leucoblastic response of the bone-marrow to supply abundance of polymorphonuclears to resist invasion.
4. Synchronous with the escape of the leucocytes is the *oozing of the lymph* into the surrounding tissues in abnormal abundance ('inflammatory œdema'), the amount of which is determined by the nature of the particular toxin causing the inflammation. The exuded lymph is richer in proteins than the ordinary lymph, and is usually coagulable.
5. Late in the process, the chromocytes, which do not possess the power of independent locomotion, are squeezed through the capillary walls, partly as the result, it is suggested, of increased intravascular pressure.
6. *Stagnation* of the blood-stream. The blood cells now cease to pass out.

The fixed tissue cells of the part undergo *cloudy swelling*, and *fatty* and *mucoid degeneration*.

Should the inflammation be very mild and the morbid agent soon cease to act, the exudate and leucocytes are absorbed by the lymphatics, the damaged cells recover, and the part resumes its normal condition.

Purposes of Inflammation.—The large lymphocytes and the polymorphonuclear leucocytes possess the power

of ingesting bacteria, and for this reason they have been named by Metchnikoff *phagocytes* (*phagein*, to eat). 'The phagocytes, having arrived at the spot where the intruders are found, seize them after the manner of the amœbæ, and within their bodies subject them to intracellular digestion.' (Metchnikoff). The migration of the leucocytes to the inflamed area thus tends to remove *the cause* of the inflammation and bring it to an end. The exuded lymph may serve two useful purposes—(i.) it may dilute the toxin, and also neutralize it by the action of its antibodies (*vide* Immunity); (ii.) it may act as a bactericide.

Other Sequels of Inflammation.

In the more severe forms of inflammation, the fixed cells of the inflamed area tend to proliferate—notably, the connective-tissue corpuscles, the vascular endothelium, and simple epithelial cells, such as those lining tubules or covering surfaces (muscle and nerve cells do not proliferate, though their nuclei may). If the inflammation persists, the derivatives of the connective-tissue cells tend to organize into fibrous tissue. Thus, all mild *chronic* inflammations tend to cause fibrosis of the inflamed tissue. The process of fibrous tissue formation does not belong to inflammation proper (see Repair). It is a constructive process, set on foot either to repair the damage which inflammation often necessarily entails, or to form a protective boundary. When, as often occurs in mild chronic inflammations, the fibrosis is apparently altogether in excess of the requirements, we have an illustration of the truth that the organism, in its efforts to do the right thing, sometimes fails.

Suppuration.—If the inflammation is of still greater severity, as when due to the pyogenic bacteria—viz.,

Staphylococcus pyogenes aureus
Staphylococcus pyogenes albus
Staphylococcus pyogenes citreus
} 75 per cent. of pus formation,

Streptococcus pyogenes
Bacillus pyocyaneus
Bacillus typhosus
} 25 per cent. of pus formation,

Bacillus coli communis,
Gonococcus,
Pneumococcus,

any of which may infect an area from the external or internal surfaces of the body, or from the blood-stream (auto-infection), suppuration may occur; the phagocytes, notwithstanding their large output from the bone-marrow, are unable to cope with the virulence of the infection: the vessels become thrombosed, the tissues are dissolved (histolysis) by the peptonizing action of the bacterial products, and *pus* is formed—*i.e.*, a fluid composed of exuded lymph and of the liquefied and digested tissue, holding in suspension dead polymorphonuclears (mononuclear pus is very rare).

Probably all cases of suppuration are due to bacteria. In the few cases in which they are not found, the likely explanation is faulty technique.

In all cases of suppuration there is an *early* polymorphonuclear leucocytosis which is of great diagnostic importance, as it can often be discovered before the patient feels ill. Accordingly we must assume that some positively chemiotactic substance exists in the blood, which stimulates the bone-marrow to the production of large quantities of leucocytes, as an ordinary sized abscess would contain all the leucocytes naturally present in the blood.

If the pus is pent up in the tissues, the condition is termed an *abscess*. If, on the other hand, the inflamed tissue yielding the pus abuts on a surface, and the skin or mucous membrane breaks, the result is an *ulcer*.

The walls of the abscess cavity are formed of 'granulation tissue.' The most superficial portion of this tissue is softer and more vascular than the underlying portion, from which it can be stripped off, and yielding, as is does, pus, is known as the *pyogenic membrane*. The outermost portion tends to organize into fibrous tissue, which, in a chronic abscess, may form a dense capsule, so that the abscess, if situated in such a structure as the mammary gland, *e.g.*, may feel like a solid tumour.

Gangrene, Necrosis, Slough.—If the inflammation is of such virulence that there is not time for the tissues to undergo liquefaction, and they die quickly *en bloc*, while still retaining their structure, the resulting state is termed *gangrene*, *necrosis*, or *slough*.

FEVERS.

The body temperature varies in different species of animals :

	F.		F.
Man	... 98·6°	Rabbit ...	... 103·1°
Monkey ...	... 100·6°	Guinea-pig ...	... 102·4°
Horse ...	... 100°	Hen	... 108°
Dog	... 102·2°		

Leucocytosis occurs in all fevers, with the exception of enteric, measles, influenza, German measles, malaria, Malta fever, dengue, and acute miliary tuberculosis. The absence of leucocytosis in lobar pneumonia usually means death.

The rash of a fever is probably due to the irritation produced by the elimination of toxin by the skin, being thus similar to the rashes sometimes found after the administration of certain drugs — *e.g.*, bromides, iodides, and copaiba.

Changes Occurring in Fever.

The *temperature* is raised. Very exceptionally this classical symptom is absent—*e.g.*, in certain cases of diphtheria, septicæmia, typhus, and enteric, when there is generally profound prostration, early coma, and death. The elevation of the temperature is in part due to increased production of heat, and in part to deficient heat loss.

The *pulse-rate* is accelerated, the average being $4\frac{1}{2}$ beats for each 1° F.

The *respiration* is accelerated, and usually maintaining the ratio in health—*i.e.*, 1 to 4—except in pneumonia and pericarditis.

The *secretions* tend to dry up—*i.e.*, those of the skin, those of the mouth, alimentary tube, liver, pancreas, and kidneys.

The *urine* is scanty, concentrated, of high specific gravity, deposits urates on cooling, and not infrequently contains albumin (febrile albuminuria).

Metabolism. — There is increased katabolism and lessened anabolism. The nitrogenous waste products, urea, uric acid, etc., are increased in quantity, as likewise is the CO_2.

Tissue Changes.—The body fat tends to disappear, the liver loses its glycogen, the muscles shrink, there is cloudy swelling of the epithelium, and often focal necrosis of the liver, spleen, and kidneys. In some fevers, notably diphtheria, there is a marked tendency to fatty degeneration of the heart. In rheumatic fever the heart (especially the left ventricle) is probably always dilated.

Death in fevers generally takes place from heart failure.

Contagion is probably conveyed via the secretions, and by these alone—*e.g.*, spraying the air during the acts of coughing, sneezing; by the evacuations, fæcal and urinary.

IMMUNITY.

By 'immunity' is meant, broadly speaking, the power which living protoplasm possesses of resisting injurious influences; in the restricted sense in which we shall employ the term, it means resistance against diseases of bacterial and protozoal origin. Life has been defined as a continual struggle against death. Hosts of invisible foes, ever ready for the attack, encompass the living organism, and were it not provided with adequate defensive mechanisms, existence would be impossible. The living body may be compared to a fort perpetually invested by the enemy's battalions, and it is only by unceasing vigilance on the part of the tissues that attacks can be warded of. Immunity, then, is a fundamental property of all living matter.

NATURE'S LINES OF DEFENCE.

Local	1. The physical resistance offered by healthy and intact skin and mucous membrane. 2. The phagocytic action of the tissue cells at the site of infection. 3. Inflammation at the site of infection.
General	4. The extermination of the bacteria by—(*a*) bacteriolysis, (*b*) general phagocytosis, (*c*) opsonins. 5. The generation of antitoxins to neutralize the toxins formed by the bacteria.

Before proceeding to discuss the subject of Nature's mechanisms of defence, it is necessary at the outset to

make quite clear that immunity involves two definite and entirely distinct factors :

(*a*) Defence *against the bacteria themselves*, and
(*b*) Defence *against the toxins they generate.*

Further, that the nature of the particular defence employed varies according to the nature of the infecting micro-organism. The following examples summarize the different modes of defence :

With tubercle bacilli and staphylococci	= phagocytosis.
With cholera and plague	= bacteriolysis.
With enteric fever	= bacteriolysis and phagocytosis.
With diphtheria	= antitoxin.

1. *The Physical Resistance offered by Healthy and Intact Skin and Mucous Membrane.*—So long as the epidermis remains healthy and unfissured, bacteria may come into contact with it almost with impunity. To a less extent, the same remark applies to mucous membranes; microbic invasion of, or through, a mucous membrane is more likely to occur when there has been a preceding catarrh, or injury, of its surface. Epithelial cells may, in a minor degree, exert a phagocytic action.

2. *The Phagocytic Action of the Tissue Cells at the Site of Infection.*—Probably all tissue cells are capable of exercising a phagocytic influence. Certainly this is so in the case of endothelial cells, especially those of the serous membranes, bloodvessels, and lymphatics. In fact, phagocytosis may be regarded as one of the primordial functions of protoplasm.

3. *Inflammation occurring at the Site of Infection.*—As pointed out in a previous page, inflammation is to be looked upon as Nature's fight against infection, for it is essentially bactericidal and antitoxic.

4. *The Extermination of the Invading Bacteria by* (*a*) *Bacteriolysis*; (*b*) *General Phagocytosis*; (*c*) *Opsonins.*

(*a*) Bacteriolysis.

By this is meant the dissolution (*lyo* = I dissolve) of bacteria by substances formed in the blood and lymph.

The epoch-making experiment of Pfeiffer is the foundation of our knowledge of the bacteriolysins.

Pfeiffer's Observation.—If a guinea-pig is immunized against cholera by injecting it with small and gradually increasing quantities of the cholera vibrios, vibrios subsequently injected into the peritoneal cavity of such an animal, first become motionless, then die, and ultimately disappear. Seeing that few, if any, leucocytes are present in the peritoneal cavity, Pfeiffer regards the substance causing these phenomena as an excretion from the endothelium lining the peritoneum, and inasmuch as it dissolves the organisms, it is spoken of as a *bacteriolysin.* Outside the body, the blood-serum of a highly immune guinea-pig has similar bacteriolytic properties.

Hæmolysins (*haima*=blood; *lyo*=I dissolve).—If the chromocytes of one species of mammal—*e.g.*, the horse—are introduced into the body of another species of mammal—*e.g.*, the dog—the latter animal elaborates a serum capable of dissolving the chromocytes of horses in general. Such a serum is said to contain hæmolysins. The serum may in a similar way be made to acquire the property of dissolving other cells, such as those of the kidney, liver, and testes, and such sera are said to contain *cytolysins* (*kytos*, a cell; *lyo*, dissolve), of which nephro-, hepato-, and spermato-lysins are examples.

Clearly, then, the occurrence of bacteriolysis depends upon the production of 'antibodies,' but this term requires explanation, and here it is necessary to offer a few remarks with reference to the terminology now employed.

Antigen.—Any foreign substance entering the tissues, be it microbe, toxin, chemical substance, or alien cell from another animal (*e.g.*, red blood cell, renal cell, spermatozoon, etc.), and giving rise to a defensive reaction therein, is known as an antigen, because it leads to the generation of special agents of defence—the antibodies.

Antibody.—The antibody consists of two parts, one of which is thermolabile (=destroyed by a temperature of 55° C.), and is known as the *alexin* or *complement*; the other (which is the antibody proper) is thermostabile (=resists a temperature of 75° C.), and is known as the *sensitizer* or *immune body* (also as the amboceptor).

The alexin, or complement, is naturally and always present in the blood and lymph of every individual, healthy or diseased; on the other hand, the sensitizer or immune body is not naturally present, being *only produced during the process of immunization;* it is specific—*i.e.*, for every antigen there is a corresponding special sensitizer, generated for the particular occasion.

The alexin is called the complement because it completes the action of the sensitizer; *one is powerless without the other.* In the following remarks the term *complement* will be employed instead of alexin.

Let A = antigen, S = sensitizer, C = complement, then—

$$A + S + C = \text{lysis.}$$

The production and action of the antibody is well illustrated in the following experiment:

Wassermann's Reaction (the Fixation Test, or Deviation of the Complement).

Antigen	*Tube* 1.—Take a piece of the liver of a syphilitic fœtus (this swarms with Treponemes). Pound and mix with sterilized water, and place in Tube 1.
Complement + sensitizer, or complement alone	*Tube* 2.—Into this place some serum from a patient supposed to be syphilitic. If syphilis is present, then the serum will contain both the ordinary complement and the specific sensitizer peculiar to syphilis. *Per contra*, in the absence of syphilis, only complement is present.
Sensitizer	*Tube* 3.—Into this tube place some guinea-pig's serum sensitized against rabbit's blood. (The guinea-pig is inoculated several times with the defibrinated red corpuscles of the rabbit. Hæmolysis takes place.) This serum contains both sensitizer and complement. By heating to 55° C. the complement is removed and the sensitizer remains.
No complement or sensitizer	*Tube* 4.—Into this tube place washed defibrinated corpuscles of rabbit's blood.

Mix contents of 1 and 2, then add contents of 3 and 4 and place in an incubator for two hours.

If the rabbit's corpuscles in 4 *remain intact* (*i.e.*, if there

is no hæmolysis), *the patient is syphilitic*, the reason being that the antigen in Tube 1 and the sensitizer in Tube 2 have united with the complement (also in Tube 2) before the addition of the sensitizer in Tube 3. No hæmolysis can take place in Tube 4 *because the comple-*

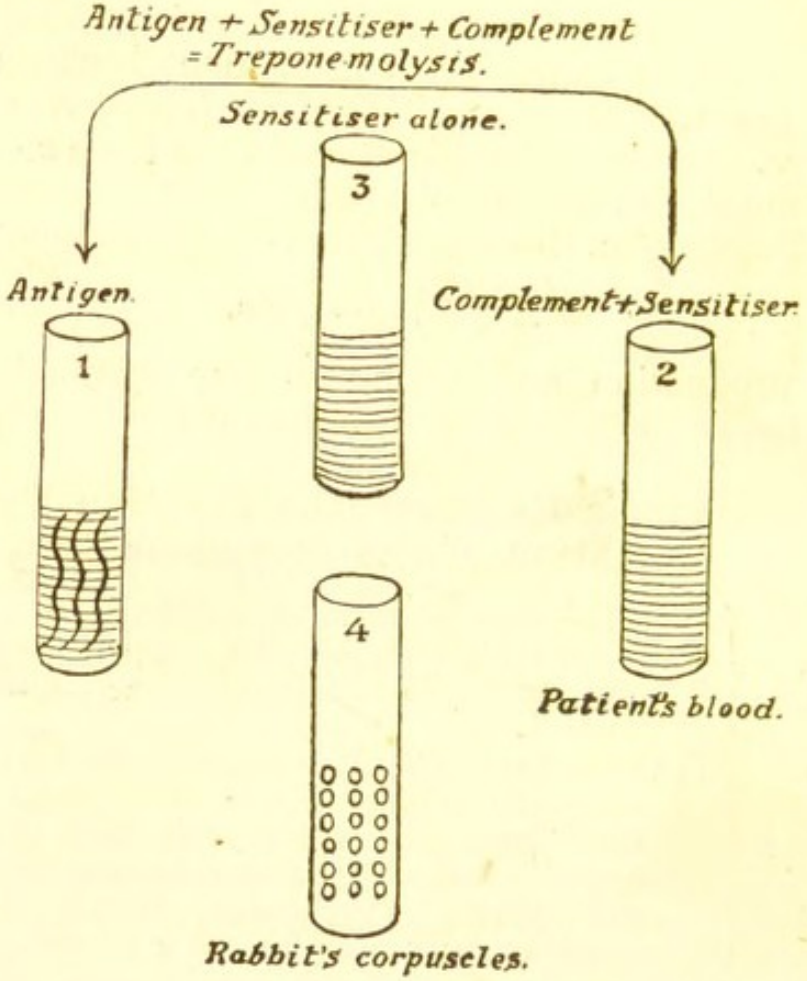

FIG. 4.

Fixation of the Complement: Treponemolysis.—The complement and sensitizer in Tube 2 attack the antigen in Tube 1, and causes treponemolysis. The complement now being 'fixed,' there is no hæmolysis in Tube 4, because the sensitizer in Tube 3 is powerless to act alone.

ment has been fixed, and the sensitizer is powerless to act alone.

In the next case, assume the patient is non-syphilitic. Mix the contents of the tubes as before, and place in an incubator for two hours.

The liquid becomes red and turbid from hæmolysis,

the reason being that the patient, not having syphilis, his blood contains no sensitizer, but it nevertheless contains complement (which is common to all bloods).

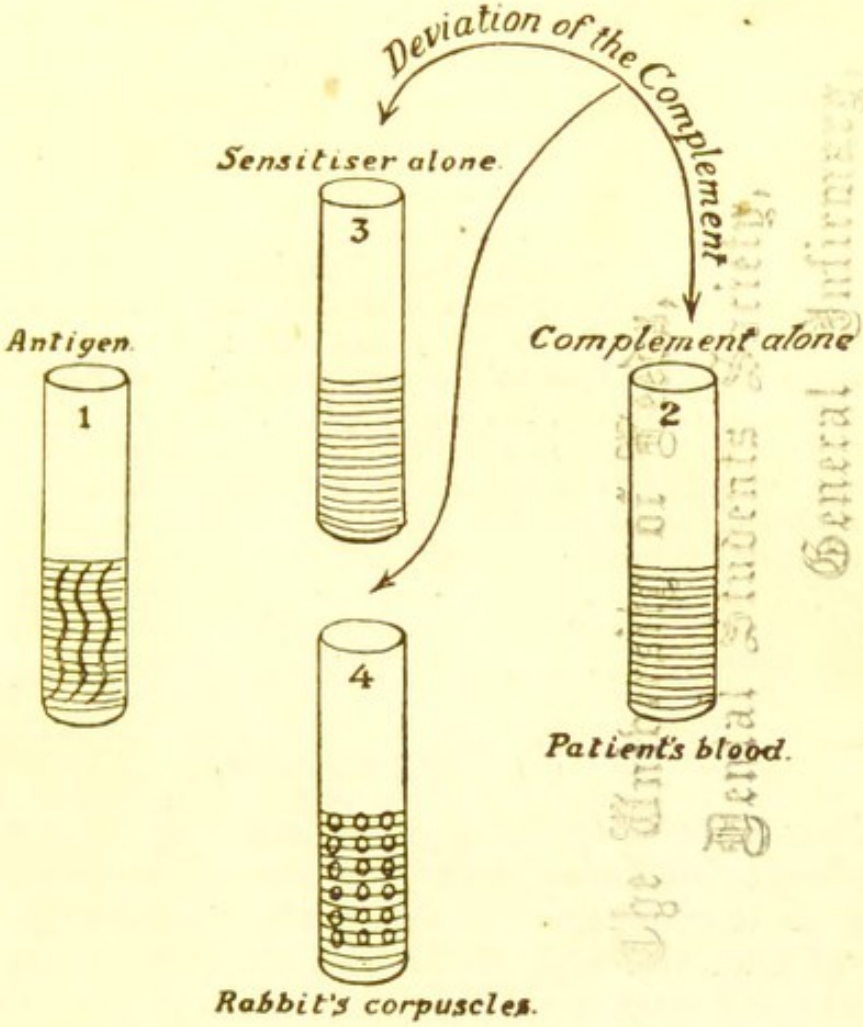

FIG. 5.

Deviation of the Complement: Hæmolysis.—The patient is non-syphilitic. The complement, which is naturally present in his blood (Tube 2) is left free, and is deviated to the sensitizer in Tube 3, so that complement in Tube 2 + sensitizer in Tube 3 = complete antibody. The complete antibody now attacks the rabbit's corpuscles in Tube 4, causing hæmolysis, hence turbidity of fluid (the rabbit's corpuscles have lines drawn through them to indicate the hæmolysis).

The complement, accordingly, in Tube 2 is free to act in conjunction with the sensitizer contained in Tube 3, hence hæmolysis in Tube 4. In this case, then, the sensitizer has caused the complement to 'deviate,' while

in the former case there is 'fixation' of the complement. For these reasons the reaction is called the *deviation of the complement*, or the *fixation test.*

The Wassermann reaction is found in about 90 per cent of cases of primary and secondary syphilis, and in the majority of cases of tertiary syphilis. It can be obtained with the cerebro-spinal fluid in about 90 per cent. of cases of general paralysis of the insane, and in about 75 per cent. of cases of tabes dorsalis.

As the result of recent researches, it has been found that an extract of normal liver (and other tissues) can be used in place of the syphilitic liver in the preparation of the antigen. This is supposed to be due to the presence in the liver of lipoids. According to Levaditi, the substances in the blood and cerebro-spinal fluid occurring in syphilis are not antibodies, but lipoids, liberated when certain tissues break down. Although this may give a new interpretation to the Wassermann reaction, it in no way militates against the value of the test in the diagnosis of syphilis. Moreover, *mutatis mutandis*, the experiment, as above described, may be taken in principle to represent, the reactions between antigen and antibodies in the production of lysis.

(*b*) Phagocytosis.

Phagocytosis (*phagein* = to eat ; *cytos* = a cell).—Metchnikoff believes that phagocytes (=leucocytes and most tissue cells) are the essential agents in the destruction of bacteria, and that the blood-plasma plays but a subordinate part in the process. 'It is the phagocyte,' he says, 'which delivers us from our enemies. Sometimes the phagocytes devour at one swoop whole masses of the organisms.' He admits, however, the existence of a complementary substance—cytase—which is probably identical with alexin.

The phagocyte, as it were, 'recognizes in the microbe a foe to the organism ; scents it from afar ; hunts, seizes, and digests it ; and then, its duty done, its mission in life fulfilled, it withdraws its pseudopodia and dies contentedly' (Adami).

If the invading bacteria are very virulent, they may kill the phagocytes, or if their spores have been taken up by the phagocytes, these may develop within the phagocytes and destroy them.

The bacteria engulfed by the phagocytes either undergo intracellular digestion or are destroyed by a chemical poison, probably related to nucleic acid and secreted by the cell nucleus.

All leucocytes possess phagocytic properties, but the polymorphonuclears and the large lymphocytes are by far the most powerful in this respect. Beside the leucocytes, most tissue cells are phagocytic, especially the endothelial cells of serous membranes, bloodvessels, and lymphatics.

Phagocytosis takes place chiefly in the blood, spleen, bone-marrow, lungs, liver, and lymphoid tissue generally.

The number of the leucocytes in the blood increases (leucocytosis), the bacterial toxin stimulating the bone-marrow to increased production of them.

Chemotaxis.—The migration of the leucocytes from the bone-marrow is explained on the hypothesis of chemotaxis, by which is meant the property possessed by a cell endowed with the power of locomotion to move towards or away from a stimulus. 'The phagocytes possess a kind of sense of taste, or chemotaxis, which enables them to distinguish the chemical composition of the substances with which they come into contact' (Metchnikoff).

In the case of the less virulent infections, the invading microbes secrete a substance which attracts the phagocytes (=*positive chemotaxis*), whereupon the latter ingest and destroy them.

In the case of virulent infections, such as the acute septicæmias, the microbes secrete a substance which repels or paralyzes the phagocytes (=*negative chemotaxis*), thus enabling the invaders to multiply without hindrance.

(*c*) Opsonins.

It was in September, 1903, that Sir Almroth Wright and Captain Douglas, I.M.S., contributed to the Proceedings of the Royal Society (vol. lxxii.) their now famous paper, in which they showed by a series of experiments that the rate and activity of phagocytosis are determined by the presence in the blood-plasma of a substance which acts on the invading bacteria 'in a manner which renders them a ready prey to the phagocytes.' To this substance (which, be it observed, is quite distinct from the bacteriolysins, etc.) they gave the name of *opsonin* (from the Greek *ὀψωνέω* and the Latin *opsōno—I convert into*

palatable pabulum), and it is distinctly to be understood that the effect they claim for it *is produced upon the bacteria* and not upon the phagocytes.

Thus, while accepting the main thesis of Metchnikoff—viz., that the final destruction of the bacteria is brought about by the phagocytes—they contend that these latter are incapable of ingesting bacteria unless these have been acted on by a substance present in the plasma, for they find that if leucocytes are separated from the blood and washed they possess little or no power of phagocytosis, but that if to the washed leucocytes blood-serum is added, phagocytosis at once takes place, thus showing that the serum contains a something which is essential to that process. Metchnikoff admits this, but he affirms that this something is derived from the leucocytes: 'Either the absorption of the microbes may be effected without the help of the opsonin, or, should such help be indispensable, the opsonin may be supplied by the leucocyte itself.'

Normal blood-plasma contains opsonin, the amount increasing with every bacterial invasion, and Wright goes so far as to assume that the body possesses the power of elaborating a specific opsonin for almost every kind of bacterium. It will thus be seen that, according to this view, the resisting power to bacteriogenic disease is largely determined by the quantity of the necessary opsonins which the host can provide. The blood of a patient suffering from bacterial invasion may contain an army of lusty phagocytes, and yet these may be powerless to attack the invaders. Their striking force will depend upon the extent to which the bacteria are first acted on by the opsonins. Just as the preliminary artillery bombardment in a battle, by demoralizing the enemy, prepares the way for the advance of the infantry, so do the opsonins prepare the way for the phagocytic attack.

Technique.—The method employed in order to ascertain the opsonic power of the blood is to mix together equal quantities of—

(*a*) 'Washed' living human leucocytes.
(*b*) An emulsion of bacteria.
(*c*) The serum containing the opsonins.

(*a*) *The 'washed' leucocytes* are obtained by taking blood from the lobe of the ear, or from the finger, and passing it into a solution of 1·5 per cent. of sterile citrate of soda in normal saline. The citrate of soda, by removing the calcium salts of the plasma, prevents clotting.

The mixture is then centrifugalized, the corpuscles thus being made to sink to the bottom of the tube, while the liquid plasma remains above. The latter is now siphoned off, and the corpuscles again washed in normal saline. Having centrifugalized for the second time, in order to sink the corpuscles, the supernatant fluid is drawn off, and the 'washed' corpuscles are then ready for use.

(*b*) *The emulsion of bacteria* is made by suspending the bacteria in normal saline solution.

(*c*) *The serum containing the opsonins* is readily procured by withdrawing blood from the lobe of the patient's ear or finger, allowing it to coagulate, and then using the expressed serum.

Equal quantities of (*a*), (*b*), and (*c*), are drawn up into a pipette and thoroughly mixed; the ends of the pipette are sealed up in the flame, and the contents incubated at the normal temperature of the human body for twenty minutes. Films are then prepared and stained in the usual way for microscopical examination.

The Count and the Opsonic Index.—On examining such a film it will be found that a number of the bacteria have been engulfed by the leucocytes (especially by the *polymorphonuclears*), and by counting the bacteria taken up by a given number of polymorphonuclears—say fifty—an average per cell can be worked out. Suppose, for example, 450 bacteria have been counted in an aggregate of fifty leucocytes, then $\frac{450}{50} = 9$ gives the average of engulfed bacteria per cell. Now perform an exactly similar experiment with the serum of a healthy man; then, if we suppose his count to average ten per leucocyte, the opsonic value, or, as it is usually termed, the *opsonic index*, of the patient's blood will be $\frac{9}{10} = 0{\cdot}9$.

The opsonic index of a patient thus expresses the power of his opsonins to influence the ingestion of microbes by phagocytes as compared with that of the opsonins of a healthy person.

It is obvious, then, that when an individual is suffering

from a bacteriogenic disease a knowledge of his opsonic index gives valuable information as to his powers of combating the disease, and that this information is essential in our endeavour to assist him by the inoculation of a bacterial vaccine.

The Opsonic Index only a Partial Measure of the Antibacterial Defences of the Body.—Wright is careful to point out that it is impossible to estimate exactly 'all the factors which make up the resisting power of the organism to bacterial invasion'—to enumerate all the leucocytes, to measure their individual phagocytic powers and the extent to which these powers are available for application,

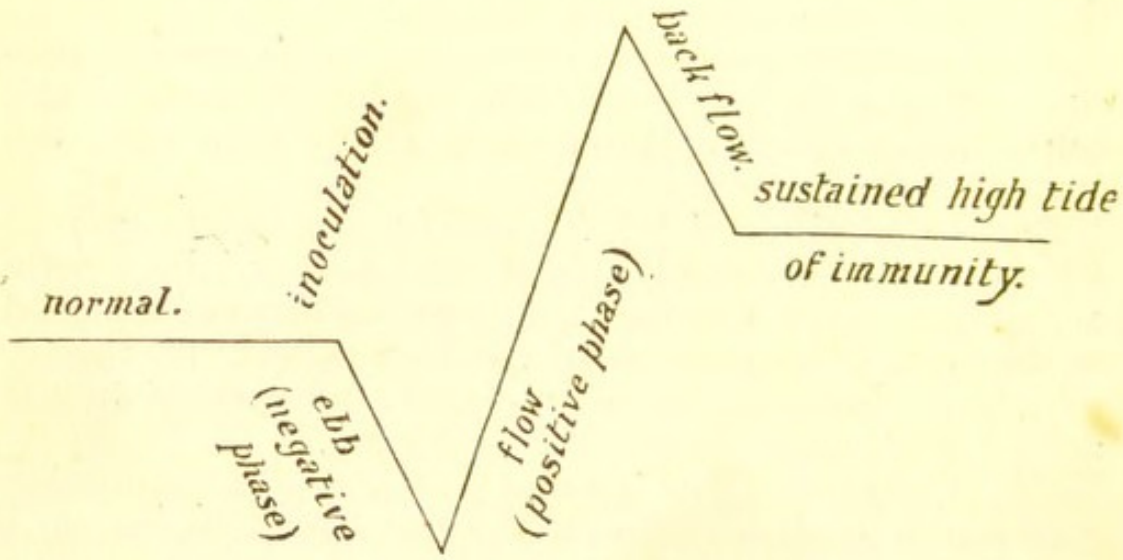

FIG. 6.

and to estimate all the known—to say nothing of the unknown—antisubstances which have affected the microbe from which the patient is suffering. The measurement of the opsonic power of the blood leads admittedly to only a partial estimate of the antibacterial defences of the body. He claims for it, however, (*a*) that it can be accurately measured, and (*b*) that it increases and diminishes in response to inoculation by vaccine and in correlation with the patient's clinical condition.

Wright's Law of the Ebb and Flow, Back Flow, and sustained High Tide of Immunity.—The first effect of a bacterial infection is to cause a fall in the opsonic index —the negative phase (*ebb*), owing to the taking up by the

bodies of the bacteria of some of the available opsonin. This is followed by a rise to a point above its original level—the positive phase (*flow*), owing to fresh supplies of opsonin being generated. A second, and this time moderate, fall then occurs (*reflow*), after which the index remains for a variable time at this higher level (*maintained high tide of immunity*).

This law holds good both for cases of ordinary bacterial infection and also for cases in which the products of dead bacteria (vaccines) are introduced into the body by inoculation.

By a series of properly timed inoculations with the appropriate vaccines, the opsonic index of the blood can be gradually increased to a level at which it tends to remain permanently high.

Antitoxins.

The influence of micro-organisms on the body depends upon the toxins which they produce.

The bacterial toxins (*toxikon*, poison) are poisonous substances allied to proteins, and, like them, possessed of a highly complex composition. Just as certain plants possess their special alkaloids (strychnine, morphine, aconitine, etc.), so each species of bacteria elaborates its own particular products, some of which may be useful to their host, some innocuous, and some harmful. It is to these latter poisonous products that Brieger gave the name of *toxins*.

It is to be understood that in speaking of the toxins of a particular bacterium we are referring to solutions of them, no toxin having as yet been isolated and analyzed as the vegetable alkaloids have been.

It is probable that there are two kinds of bacterial toxins:

(*a*) Those confined to the interior of living bacteria and only liberated on their death of them (*intracellular*, or endo-toxins); and

(*b*) Those yielded by living bacteria to the medium outside them (*extracellular*, or exo-toxins).

(*a*) *Intracellular Toxins.*—In this group, which includes the toxins of the greater number of bacteriogenic diseases, amongst others those of lobar pneumonia, enteric fever, Malta fever, cholera, plague, and gonorrhœa, the toxin is intimately bound up with the protoplasm of the bacteria, not being liberated till these degenerate or die, and then only when the bacilli disintegrate. It is found, in the particular diseases just referred to, that if the bacteria causing them are grown in a suitable

culture medium no toxin separates out by filtration through porcelain, whereas if the bacteria are frozen at the lowest of temperatures and then crushed, the result is a highly toxic substance.

(*b*) *Extracellular Toxins.*—In this group, which includes the toxins of diphtheria and tetanus, the toxin appears to be of the nature of an excretion. If, for example, the diphtheria or the tetanus bacillus is grown in a suitable medium *soluble toxins are found to pass out into the medium, from which they can be separated by filtration through porcelain*, the inference being that the bacilli in question excrete them (unless we suppose that they produce them by promoting some change in the external medium).

Some species of bacteria appear to produce both intracellular and extracellular toxins—*e.g.*, tubercle bacillus (probably).

Ehrlich assumes that a molecule of toxin consists of two groups of atoms: one the *haptophore* [(*h*)*apto*=I fasten], which combines with the antitoxin; and another, the *toxophore*, on which the toxic action depends (see diagram of Ehrlich's side-chain theory, Fig. 7). For example, if diphtheria toxin be kept for some time it loses its toxic property, but retains its power of combining with antitoxin—it has lost its toxophore, and retained its haptophore, group of atoms. Such a toxin Ehrlich calls a *toxoid*.

Action of Toxins.—Toxins appear to unite with the protoplasm of the tissues. In many of their properties, however, they resemble ferments. Thus:

They are destroyed by a temperature of from 140° to 212° F. They are precipitated by alcohol; they are unaffected by chloroform and ether. They can be swallowed with impunity. They do not act until after a latent period. They act irrespectively of the quantity employed; *i.e.*, an infinitesimal dose is effective; *e.g.*, $\frac{1}{1000}$ gramme of tetano-toxin will kill a horse 600,000,000 times its own weight.

Fate of Toxins.—Ultimately toxins are partly excreted as such (chiefly by the kidneys and liver), partly burnt up in the tissues, and partly neutralized by antitoxin.

An *antitoxin* is a specific substance elaborated by the blood, lymph, or tissues, as the result of the presence in the body of a toxin. The antitoxin and the toxin together probably form an inert chemical compound. If a horse is injected with progressively increasing sublethal doses of the toxin of the bacillus of diphtheria, a serum rich in antitoxin can then be obtained from the animal, which is capable of neutralizing the toxin circulating in the blood of a patient suffering from diphtheria. That the neutralizing antitoxin acts upon the bacterial toxin, and not upon the

bacteria themselves, is proved by the fact that *the bacilli of diphtheria will grow readily in diphtheria antitoxin.* If a similar experiment be performed, but tetanus-toxin used instead of diphtheria-toxin, it is found that the resulting tetanus-antitoxin is not an antidote for diphtheria-toxin, nor *vice versa. Each antitoxic serum, then, is specific*, neutralizing only the toxin of the corresponding organism.

It is to be clearly understood that by administering an antitoxin the *free* toxin only is neutralized. Hence the *urgent need of giving the antitoxin early*, for the toxin which has entered into combination with the tissues is beyond the reach of the remedy. In the treatment of tetanus, for example, antitoxin is of little practical value unless immediately injected into the nerve leading from the wound, for the tetano-toxin rapidly disappears from the blood and travels along the axis cylinders of the nerve to the central nervous system, to the elements of which it becomes 'fixed,' thus being inaccessible to the action of the injected antitoxin.

The mortality from diphtheria in the hospitals of the Metropolitan Asylums Board (London) has fallen from above 30 per cent. to less than 10 per cent. since the introduction of the antitoxin treatment of this disease.

Ehrlich's Hypothesis of Antitoxin Formation.

Bacterial toxins are, as already stated, allied to proteins and as such possess a highly complex chemical composition, in contradistinction to the ordinary chemical poisons, such as the vegetable alkaloids—*e.g.*, strychnine and prussic acid. These two classes of poisons further differ as regards their chemical action on the tissues, the former entering into more intimate chemical union with them than the latter—so much so that, while it is impossible to recover a bacterial toxin, such as that of tetanus, from the tissues after death, it is quite possible to recover such poisons as strychnine and prussic acid. This, according to Ehrlich, is because the former class of poisons enter into firm chemical union with the living protoplasm, being actually built up into or assimilated by it, while the latter unite only with the fatty and other substances entangled

in the protoplasmic network, and not with the actual protoplasm itself.

Ehrlich assumes that the molecules of which protoplasm is constituted consist of a central part furnished with numerous side-chains or 'receptors,' adapted to unite with,—'fitting like a key fits a lock'—and thus assimilate the various food-stuffs circulating in the tissue plasma, there being protein-receptors (P) for proteins, carbohydrate-receptors (C) for carbohydrates, fat-receptors (F) for fats, and so on.

Now, when toxins are present they, being allied to certain food-stuffs, are, as it were, mistaken by the tissues

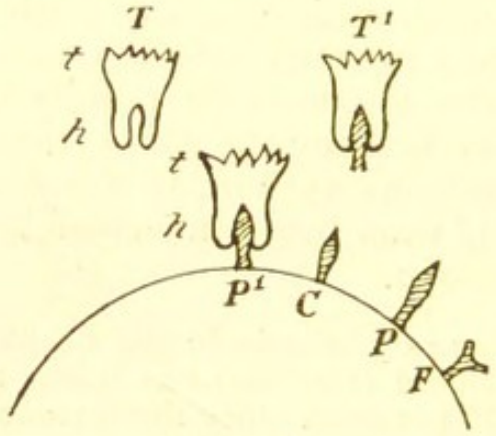

FIG. 7.

P = Protein-receptor; C = carbohydrate-receptor; F = fat-receptor; T = toxin molecule, with haptophore (h) and toxophore (t); P^1 = protein-receptor linked to haptophore; T^1 = toxin molecule detached from cell, with protein-receptor linked to it.

for them, and are caught up by receptors specially adapted to receive them.

If the receptor possesses no affinity for the toxin, the animal will be naturally immune. Imagine, however, a cell to be attacked by a toxin for which it has affinity. As already explained, the toxin molecule (T) consists of two groups of atoms: a combining group, the haptophore (h); and a poisoning group, the toxophore (t). The haptophore becomes joined to a toxophile receptor, and the toxophore then exerts its poisoning influence.

In this way a certain number of the receptors are thrown out of action, and are no longer available to carry on the

nutrition of the cell. In addition to this, the cell is partially poisoned. Under the stimulus of the morbid assimilation, the cell protoplasm buds off fresh receptors to meet the extra demand, the cell, in course of time becoming educated, so to speak, to produce an abundance of receptors, some of which are in excess of its needs. The surplus receptors are then cast off, and though free of the parent cell, still retain their power of combining with toxin. *These surplus receptors it is that constitute the circulating antitoxin*, which, by uniting with the toxin, neutralizes it, and thus protects the living protoplasm from its action. In this way life tends to be prolonged until the organism has had time to destroy the bacteria from which the toxin had its origin.

Should receptors not be formed in sufficient number, the animal dies.

Agglutinins.

If the serum of a patient convalescent from enteric fever be added to a living culture of the *Bacillus typhosus*, the organisms lose their motility and become massed into clumps (Widal's reaction).

This phenomenon is known as 'agglutination,' and is supposed to be due to the development in the lymphoid tissues, bone-marrow, and spleen of a substance—agglutinin—which, by affecting the surface tension, causes the clumping. In this respect it is analogous to the running together of bubbles on the surface of a fluid.

The process of agglutination does not appear to play any important part in immunity. It is not a certain test for the existence of enteric fever, in some cases failing to give it; moreover, it is found in Malta fever and in the dysentery due to Shiga's bacillus.

Precipitins.

If an old culture of typhoid bacilli be filtered, and the filtrate be then added to some typhoid serum, a precipitate forms. Such a precipitating substance is known as a 'precipitin.'

Precipitins are allied to, if not identical with, agglutinins, and, like these latter, probably play no important part in immunity.

Aggressins.—If a mixture of tubercle bacilli with sterilized tubercular exudate is injected into the peritoneum of a guinea-pig, the animal dies rapidly. If, however, each be injected separately, nothing happens. From this Bail argues that there is something in the

exudate which increases the virulence of the bacteria by paralyzing the phagocytes (negative chemotaxis), and thus permitting the invading microbe to exist without hindrance. To this specific substance, formed by the bacteria to inhibit phagocytosis, he gives the name of 'aggressin.' On this hypothesis, immunity depends upon the production by the body of anti-aggressins, which, by neutralizing the aggressins allows the phagocytes full scope as agents of defence.

Susceptibility.

Natural Susceptibility.—If a mouse is inoculated with anthrax at the tip of its tail, even though the tail be amputated within one minute of the inoculation, the animal will succumb to anthrax—a striking instance of natural susceptibility.

Man is similarly susceptible to certain bacterially induced diseases, such as hydrophobia and syphilis.

Acquired Susceptibility.—The hen is naturally insusceptible to anthrax; when, however, its feet are immersed in cold water it becomes susceptible, and experiments have proved that not only cold, but hunger, thirst, improper feeding, fatigue, and loss of blood, all tend to increase susceptibility to bacteriogenic diseases. White rats, for example, which are ordinarily insusceptible to anthrax, become susceptible after fatigue, or when fed upon a purely vegetable diet. Again, while healthy swine do not contract glanders, young and debilitated pigs may sometimes be affected with it.

Immunity may be—

(*a*) Natural, or
(*b*) Acquired.

(*a*) **Natural Immunity.**—This in some cases has been achieved by natural selection. In this way a race may become completely or partially immune as regards a disease to which its ancestors were highly susceptible. It is probable, however, that the susceptibility of a species to bacterial infection essentially results from *the bacterial parasite having acquired the power to infect;* and when a species is immune as regards a particular bacterium, it

may be, and in all probability generally is, because this latter has not acquired the power of establishing a lodgment in that species. Rinderpest is essentially a disease of ruminants; horses never contract it. Tuberculosis, though common in cows and pigs, is very rare in horses, asses, sheep, goats, and dogs. Again, Algerian sheep are immune against anthrax, although ordinary sheep are susceptible to this disease.

Immunity, like susceptibility, is a *relative* term. With few exceptions, no animal which has been made the subject of observation possesses absolute immunity against any given microbial disease, under every possible circumstance.

(*b*) **Acquired Immunity.**—Of this there are two chief kinds:

(*a*) Active or Direct.
(*b*) Passive or Indirect.

(*a*) *Active Immunity.*—Examples of this are—

1. Immunity due to a previous attack of an infectious disease—*e.g.*, measles, scarlatina, mumps.

2. Immunity due to inoculation with small doses of the specific *virus* of a micro-organism that has been passed through the body of another animal, as in the case of vaccination for smallpox.

3. Immunity due to repeated inoculations with sub-lethal doses of *living micro-organisms*, which in course of time produce an immunizing substance in the blood, so that the animal can ultimately tolerate a dose which would at first have been fatal, as in the case of Pasteur's method for fowl cholera (now seldom employed).

4. Immunity arising from inoculation with the serum of an artificially immunized animal—*e.g.*, anti-diphtheritic serum.

(*b*) *Passive Immunity.*—If the blood-serum of an animal rendered immune against a particular disease—*e.g.*, diphtheria—by any of the above methods is injected into a second susceptible animal, this animal also becomes immune against that disease. In such cases the process of immunization is *passive* so far as the second animal is concerned. An infant fed at the breast is less liable to contract disease than one brought up by hand, one reason

for this being that it derives immunizing substances rom its mother's milk, and in this way is rendered passively immune.

Symbiosis.

Symbiosis, or mixed infection, has a marked influence on the course of bacteriogenic disease. For example, the presence of staphylococci and streptococci in the fauces augments the virulence of the bacillus of diphtheria. Again, without the presence of an aerobic organism, such as the *Staphylococcus pyogenes*, the bacillus of tetanus cannot develop in a wound.

Mixed infection occurs to a large extent in respiratory and alimentary diseases and profoundly influences their course.

Vaccines.

A vaccine (*vacca* = a cow) is an attenuated virus which, when injected into the body, induces there the development of some protective substance (or substances), the effect of which is either to render the organism insusceptible to a particular disease (= active immunity) or to mitigate its severity if incurred. The fundamental principle of vaccine-therapy, to quote Sir Almroth Wright again, 'is to exploit in the interest of the infected tissues the unexercised immunizing capacities of the uninfected tissues.'

The vaccines in general use are watery emulsions of bacterial cultivations, containing either bacterial products (but no living bacteria—*e.g.*, Koch's tuberculin consists of a suspension of dead tubercle bacilli), or a living culture of mitigated virulence.

The result of inoculation by appropriate vaccines is definitely to raise the opsonic index, and in this way to increase the capacity of the organism to resist the growth of the specific microbe.

'The injection of the vaccine, if the dose be properly adjusted, leads to the development locally of antibacterial substances in quantities more than sufficient to neutralize the bacteria or bacterial substances introduced, leaving a surplus which can be carried by the blood and lymph to other parts to augment the resistance offered to the original infection. The response to the inoculation of a vaccine can be studied in various ways: first, the production of antibacterial substances can be measured by

studying the opsonins or other antibacterial substances evolved; secondly, the effect of the injection upon the clinical manifestations of the infection—the local lesions—upon the temperature chart and upon the general condition of the patient may be observed. Vaccines have now been employed in the treatment of a large number of infections, both general and local, with results sufficiently encouraging to warrant the hope that this method of treatment will prove to be of general application and utility. In some instances—for example, in furunculosis and other localized staphylococcal infections, and in cystitis and other infections of the urinary tract due to the colon bacillus—the results have been most striking, so that, apart from questions of dosage and methods of control, this form of treatment has practically passed beyond the stage of controversy in these conditions. In regard to many other diseases, it is still in the experimental stage, but in some of these, such as pneumonia, typhoid fever, gonococcal infections, septicæmia, and endocarditis, encouraging observations are on record. Sir William B. Leishman, in his contribution to the discussion (at the Royal Medical Society), referred to some observations made under his direction concerning the therapeutic applications of typhoid vaccines with results that he regarded as distinctly encouraging. In some forms of septicæmia and infective endocarditis vaccine-therapy appears at present to offer the only hope of success, and in such conditions it is being extensively tried. In regard to tuberculous infections, there is considerable difference of opinion. By some writers tuberculin in one or other of its many forms is hailed as being of the utmost value, while by others its use is condemned. From published cases it appears to be of value in localized tuberculous lesions, including those of the skin and glands. In regard to pulmonary tuberculosis, no general consensus of opinion has yet been arrived at. It is used in many sanatoriums, and statistics are on record of cases treated with it giving greater proportions of successful results with longer periods of freedom than in cases not so treated' (*Lancet*, September 24, 1910).

Gangrene.

By *gangrene* is meant the death of the *soft* tissues in mass.

Classification.

- From destruction of the tissues outright
  - Burns, corrosive poisons, etc. Septic inflammatory gangrene is probably in part due to the direct destructive action of the toxins on the protoplasm of the tissues.
- From vascular obstruction
  - Arterial
    - Rupture, ligature, embolism, or thrombosis of main artery; arterial spasm (*e.g.*, from ergotism, frost-bite, Raynaud's disease).
  - Venous
    - Tight bandage, plaster of Paris, splint-pressure, thrombosis, strangulated hernia.
- From acute septic inflammations
  - Carbuncle, cancrum oris, sloughing phagedæna, malignant œdema, malignant pustule.
- From interruption of trophic influence
  - Acute bed-sores after injuries to spinal cord.

Clinically there are two main varieties of gangrene—the 'dry' and the 'moist.' The former only occurs when the arterial afflux is obstructed, as when a main artery is thrombosed or plugged with an embolus; the latter when the venous efflux is obstructed, as from thrombosis of a main vein. All gangrenes resulting from inflammations are of the 'moist' variety.

Dry Gangrene is well illustrated in the case of the ordinary variety of *senile gangrene*. The arteries of the leg, narrowed and rigid from calcareous degeneration, become gradually thrombosed, and the blood-supply being thus cut off, the part presents a tallowy white colour. Later on it becomes purple or mottled, owing to extravasation of hæmoglobin from the vessels. In consequence of the evaporation which takes place from the surface, the tissues become dry and shrivelled, and the skin assumes the appearance of parchment, ultimately becoming covered with an oily film from transudation of the underlying fat.

If the process is arrested, the dead part acting as an irritant to the adjacent living tissues, a dusky red zone

of inflammation forms, called *the line of demarcation.* Finally, the dead part is separated from the living by suppuration.

Constitutional infection is rare in dry gangrene, the dried up, shrunken tissues not providing a suitable soil for the growth of organisms.

Moist Gangrene is well illustrated in cases of septic inflammatory gangrenes. The vessels are thrombosed as the result of toxic action, and the gangrenous part becomes soaked in an albuminous fluid containing many disintegrated chromocytes. The dissolved-out hæmoglobin, diffusing itself through the dead tissues, stains them a greenish-black (= FeS). Later on, *bullæ*, containing a blood-tinged fluid, form. Still later, gases are generated from infection by the *Bacillus aërogenes capsulatus* of Welch, giving rise to emphysematous crackling. Ultimately the part putrefies, and constitutional infection occurs.

Gangrene from Embolism.—This is commoner in the leg than in the arm, the latter having a freer collateral circulation. The embolus generally lodges at the bifurcation of the popliteal artery. The gangrene is at first always of the 'dry' kind: the limb assumes a tallowy colour, and becomes cold, numb, and insensitive, with arrest of pulsation in the artery below the seat of obstruction.

Should the part become septic, the gangrene changes into the 'moist' variety.

Gangrene from Ligature of an Artery.—This, though possible, rarely results from a ligature *per se*, there being usually an associated thrombosis of the companion vein as the result of injury at the time of the operation. Hence the gangrene is generally moist.

Raynaud's Disease.—Vaso-motor spasm affecting the outlying cutaneous vascular regions (hands, feet, nose, ears) is very common. In the hands, especially, every degree of spasm may be observed, from slight temporary blanching to spasm so severe and protracted as to cause actual gangrene.

Transient spasm of the fingers causes them to become suddenly pale or tallow-like. This condition is known as 'dead fingers,' and is common in women during the reproductive period of life. It is probably associated with the vaso-motor fluctuations peculiar to menstruation.

A protracted spasm of the hands and feet causes them to become cyanotic. This is the condition obtaining in those who suffer much from cold hands and feet. It is nearly as common in men as in women, and, although a purely local phenomenon,

is popularly supposed to indicate a 'feeble circulation' of cardiac origin. The cyanosis results from the sluggish capillary circulation consequent on the arteriolar spasm; the sluggish flow allows deoxygenation to proceed beyond the normal, and the capillary blood thus becomes blue. In course of time the soft tissues of the affected region thicken, apparently from fibrous overgrowth, just as happens in the case of the sluggish capillary circulation characterizing passive congestion. It is only in minor degrees of this condition that chilblains are apt to occur.

Raynaud's disease was first described by Raynaud, under the name of 'La gangrène symétrique des extrémités.' It is more common in women than in men, and occurs most frequently between the ages of eighteen and thirty. Characteristic features are its symmetry and periodicity. In typical cases there are, as described by Raynaud, three stages:

(*a*) Local syncope (pale stage).
(*b*) Local asphyxia (blue stage).
(*c*) Local gangrene.

(*a*) *Local Syncope.*—The fingers (or toes) become cold, white, and 'dead' (=severe spasm of peripheral arterioles).

(*b*) *Local Asphyxia.*—The fingers now swell (from increased exudation through the damaged capillaries), and become of a livid colour (from excess of deoxygenated blood) and very painful.

(*c*) *Local Gangrene.*—Blebs form, and these on bursting expose small superficial sloughs, seldom extending deeper than the skin. The resulting ulcers are sluggish, and slow to heal.

The attack may stop at stage (*a*) or (*b*).

The initial event is a severe arteriolar spasm of the affected areas, to be followed by dilatation.

The attack is probably caused by the action of some vaso-constrictor toxin, generated either in the alimentary canal, uterus, ovaries, or Fallopian tubes, or as the result of some vicious metabolism of the tissues.

Frost-Bite.—The first effect of severe cold is arterial spasm, the part becoming bloodless and shrivelled. Should the exposure continue, the part dies. If, however, the patient be brought into warm surroundings before this occurs, the blood may enter the frozen part, and all the phenomena of inflammation may occur. Such inflammation may either end in resolution or in 'moist' gangrene.

Gangrene from Ergotism.—This is only found in those countries in which rye bread is eaten. If the arterial spasm induced by the ergot continues for a long time, the gangrene is dry; but should it be succeeded by vaso-dilatation, or the part become septic, the gangrene is moist.

Carbuncle.—This is due to inoculation with the *Staphylococcus pyogenes aureus* of patients with lowered vitality—*e.g.*, from

under-feeding, over-feeding, chronic alcoholism, albuminuria, and diabetes mellitus. It is most common in men over forty, and is generally situated at the lower part of the nape of the neck. It begins with *a primary inflammation of the subcutaneous tissues*, the skin being secondarily involved. At first there is noticed a rounded dusky red swelling, hard to the feel, and with well-defined margin. Soon a number of pustules form on the surface, which bursting, leave the skin riddled with pus-exuding apertures. Many of the apertures coalesce, and so expose the underlying ashy-grey slough. This is ultimately thrown off, often laying bare muscle or fascia. Healing is slow. The average size of a carbuncle is about 2 inches in diameter, but it may cover an area as large as a soup-plate.

Bedsores.—There are two kinds of bedsores, the *ordinary* and the *acute*.

The *ordinary* bedsore forms in parts exposed to pressure when the patient is in the recumbent position, the usual positions being the sacrum, the trochanters, the elbows, the spines of scapulæ, the malleoli, and the heels. It is particularly liable to develop in the old and feeble. Negligent nursing (leading to contamination with urine and fæces) is an important contributory cause. The affected part becomes red, small blisters form, and finally sloughing and ulceration supervene. In severe cases the underlying bone is exposed. The dangers are from spinal meningitis and septicæmia.

Acute Bedsore.—This occurs in a case in which a part has been deprived of nerve influence. It is typically seen after fracture-dislocation of the spine. The gangrene is moist; it comes on very suddenly, and spreads rapidly.

Cancrum Oris.—This is a quickly spreading inflammatory gangrene, attacking the inside of the cheek of unhealthy children convalescent from some specific fever, notably measles. The cheek becomes red and brawny. On opening the mouth a slough is observed. This on separating leaves a foul, excavated ulcer, which may perforate the cheek and destroy a large portion of it. The gangrene sometimes extends to the gums and the floor of the mouth. It is a very fatal malady. Should recovery take place, a serious deformity of the face is usually left.

Malignant Œdema.—This is due to the inoculation with the *bacillus of malignant œdema*. It is the most virulent and fatal form of inflammatory gangrene known. The injured part rapidly swells and becomes dusky red. This is quickly replaced by a blackish-purple discoloration, which is immediately followed by emphysematous crackling, owing to the generation of putrefactive gases. So speedily does the inflammation spread that the trunk may be involved within a few hours. The infection seems to be carried by the lymphatic vessels, which can be seen as thin red lines in advance of the inflamed margin. Inasmuch as the lymphatics are most abundant on the inner

aspect of the arm or leg, the advancing line of gangrene is most marked in these positions.

Malignant Pustule.—This, which is met with amongst workers in foreign wools and hides, is due to the inoculation of some exposed part of the body with the *Bacillus anthracis*. The patient either scratches or pricks himself, and after a short period of incubation a red pimple—suggestive of the sting of an insect—appears. The pimple enlarges, and at its centre a vesicle forms, which, bursting, leaves a scab. The margins of the 'pustule' are now indurated, the surrounding tissues œdematous, and the lymphatic glands enlarged. A second crop of vesicles soon form in the indurated margin, the central black scab meanwhile becomes dry and sunken below the level of the surrounding parts. In the course of a few days the malignant pustule attains the size of a florin, and presents the following four zones:

(*a*) A central depressed black scab.
(*b*) A zone of vesicles.
(*c*) A zone of dusky red induration.
(*d*) A zone of œdema.

The danger to life is from general infection (*anthracæmia*).

Sloughing Phagedæna.—This, which in the pre-antiseptic days was very common under the name of 'hospital gangrene,' is now, happily, very rare. Although it may complicate any wound, it is at the present day chiefly met with in cases of venereal sores. The tissues at the infected site become acutely inflamed, and a central grey slough soon appears surrounded by an angry red margin. When the slough separates, a foul, excavated ulcer is left. A large area of tissue may be destroyed in this way.

Diabetic Gangrene.—*Vide*, p. 168.

ŒDEMA AND DROPSY—THROMBOSIS—EMBOLISM.

Œdema and Dropsy.

All the tissues are bathed in a fluid—lymph—which is a very dilute kind of blood-plasma (see table). The lymph is continually oozing through the thin capillary walls and diffusing itself slowly among the tissues, to which it supplies the various substances needful to their vitality; it collects the waste products of metabolism, and ultimately flows into the venous system by the thoracic ducts.

Though the question is not yet settled, we may pro-

visionally assume that the separation of the lymph from the blood is in part—

Physical { Filtration. / Osmosis. / Dialysis.

and in part—

Vital { The endothelial cells of the capillary walls actively secrete the lymph from the plasma.

An undue accumulation of lymph in any part of the body is known as dropsy. When the fluid accumulates between the individual cells of a tissue, causing it to swell and to become puffy, the condition is termed 'œdema.'

Œdema of the subcutaneous tissues is known as *anasarca;* dropsy of the lateral ventricles of the brain as *hydrocephalus;* of the peritoneum as *ascites;* of the pleura as *hydrothorax;* of the pericardium as *hydropericardium;* and of the tunica vaginalis as *hydrocele.*

The degree of œdema is determined by the looseness or denseness of the tissue affected—*e.g.*, the subcutaneous tissues and the lungs are capable of great distension, whereas the solid organs possessing dense capsules, such as the kidneys and testes, can swell but little.

Dropsical fluids are much richer in proteins than is normal lymph (see table).

The following table from Halliburton shows the composition of dropsical fluids as compared with the normal fluids of the body:

Fluid.	Parts per 1,000.			
	Solids.	Water.	Proteids.	Salts.
Blood-plasma	97·10	902·90	82·89	8·55
Normal lymph ...	13·66	986·34	3·37	8·78
Pleuritic fluid	36·05	963·95	28·50	7·55
Ascitic fluid	39·51	960·49	29·73	5·94
Hydrocele fluid ...	61·15	938·85	50·05	9·26

Theories to explain Dropsy.—Dropsy was originally thought to be due to an abnormally watery condition of the blood, but that this *per se* is incompetent to cause dropsy is proved by the fact that the injection of large quantities of salt solution does not produce it.

The chief causes of dropsy may be classed as *mechanical* and *toxic*.

Mechanical.—Examples of this are: tight bandages applied to the arm or leg (and thus interfering with the return of blood from the veins which are more easily compressible than the arteries); pressure of enlarged glands in axilla; failing compensation in heart disease; obstruction to the portal circulation in the liver (cirrhosis, cancer), causing ascites.

Toxic.—This cause operates in such diseases as nephritis and beri-beri. It is supposed that the toxin causes some *damage to the endothelium of the capillary walls, whereby their permeability to fluids is increased*, certain capillaries, such as those of the face, being more susceptible to this influence than others. Hence the early occurrence of œdema of the face in Bright's disease (see chapter on Kidneys).

Acute Circumscribed Œdema (Angio-neurotic) is characterized by the sudden appearance of transient, sharply defined, tense and shiny œdematous swellings on the eyelids and other parts of the face, hands, genitals, or other parts. It was first described in 1880 by Quincke, and would appear to be due to some form of alimentary toxæmia.

Thrombosis.

Thrombosis (*thrombos*, a clot) means the coagulation of blood, *during life*, in any part of the cardio-vascular system—heart, arteries, capillaries, or veins; the resulting clot is called a *thrombus*.

The essential primary change in the formation of a thrombus appears to be the accumulation and fusion into a mass of blood-platelets, and their adhesion to the damaged vascular lining. According to Greenfield, the leucocytes usually take no active part in thrombus formation.

Causes.—Changes in the vessel walls; changes in the composition of the blood; retardation of the blood-flow.

Frequently two or all of these causes co-operate.

Changes in the Vessel Walls.—Damage to the endothelial lining of the vessel walls is the most important factor here. Atheroma, primary calcification, varix, phlebitis, etc., do not cause thrombosis, *unless the endothelial lining is injured or destroyed.*

Changes in the Blood.—These are such as cause *increased coagulability.* For example, in 1 out of every 100 cases of enteric fever, and in 1 out of every 150 cases of lobar pneumonia, thrombosis of the femoral vein occurs. This may be in consequence of increased coagulability of the blood, or, on the other hand, it may be the result of damage to the endothelial lining by the bacterial toxins.

Certain poisons may also operate *by increasing the fibrin-ferment—e.g.*, toxins, proteoses, snake-venom.

Changes in the Blood-Flow.—Retardation, or even arrest, of the blood-flow is by itself incompetent to cause thrombosis, for it has been proved that if a bloodvessel is ligatured in two places under strict antiseptic precautions, and care is taken not to injure the endothelial lining, the stagnant blood may remain fluid for weeks or even months together. Nevertheless, it is an important contributory factor in thrombosis. Witness the effect of compressing or ligaturing the artery supplying an aneurism, and the tendency to thrombosis of the intra-cranial venous sinuses when the circulation is languid, as in the aged and moribund, and again the clotting of blood within the auricular appendices in mitral stenosis.

Thrombosis occurs most frequently in the *veins.* Venous thrombosis is fifty times more common in the leg than in the arm.

Septicæmia, pyæmia, and other infective diseases, would appear to cause thrombosis, in part by increasing the coagulability of the blood, and in part by damaging the endothelial lining of the bloodvessels.

Appearance of a Thrombosis.—If it forms slowly, it is laminated and of greyish-white colour (=pale thrombus); if it forms quickly, it is non-laminated and red (=red thrombus). Intermediate forms may occur.

Post-mortem clots differ from thrombi in being softer, never laminated, and non-adherent to the vessel walls.

Sequels of Thrombosis:

Absorption.
Organization.
Calcification (phleboliths).
Disintegration, causing aseptic emboli.
Septic infection. This results from disintegration (*e.g.*, by suppuration) of the thrombus and the formation of septic emboli.

Embolism.

Embolism signifies the lodgment of some solid substance, or of an air-bubble, in a vessel too small to allow it to pass on. The impacting body is carried into position by the blood-stream, and is called an *embolus*. Emboli occur in the arteries, as these diminish in size in the direction of the blood-flow; also in the intra-hepatic branches of the portal vein, which, within the liver, divides like an artery. They are most frequently observed in the splenic, renal, and cerebral arteries.

An embolus of a systemic artery is derived from the left heart or systemic arteries; an embolus of the pulmonary artery is derived from the right heart, or systemic veins. A very small embolus may pass through the pulmonary capillaries into the general circulation.

Varieties:

Embolus consisting of a detached portion of a thrombus.

Embolus consisting of a vegetation detached from a heart-valve.

Embolus from detachment of an atheromatous patch in an artery.

Embolus from detachment of a portion of a tumour (*e.g.*, sarcoma).

Embolus consisting of masses of vegetable parasites (*e.g.*, *Bacillus anthracis*).

Embolus consisting of animal parasites (*e.g.*, *Filaria sanguinis hominis*).

Fat emboli.

Air emboli.

Effects of Embolism.—If the collateral circulation is sufficient to compensate for the obstruction, as in the case of the muscles, skin and bone, secondary thrombosis takes

place on each side of the plug, and extends up and down the blocked vessel as far as the nearest branches. The clot then organizes, and a small portion of the artery becomes obliterated, but the tissues do not suffer in nutrition because the collateral vessels carry on the circulation.

If a large and important vessel, such as the pulmonary or coronary artery, is blocked, sudden death may result.

If the collateral circulation is insufficient to compensate for the obstruction, the nutrition of the blocked area suffers, and the degenerated area of tissue, thus bereft of its normal supply of blood, is spoken of as an *infarct.*

Infarcts.

'End' or 'Terminal' Artery.—By this is meant an artery which, though it has *capillary anastomosis,* has no *free arterial anastomosis with neighbouring vessels.* Such arteries exist in the spleen, kidneys, intestines, brain (base), spinal cord (grey matter), retina, heart (coronary arteries). The peripheral branches of the pulmonary and superior mesenteric arteries are also to some extent end-arteries. It should be noted that the hepatic arteries are not end-arteries. An end-artery generally supplies a cone-shaped area of tissue, the base of the cone being on the surface of the organ.

An **infarct** (*farcio,* I stuff) may be defined as a degenerated mass of tissue supplied by an end-artery which has been blocked by an embolus (and sometimes by a thrombus). The affected area is usually cone-shaped, the base of the cone being at the surface of the organ, and the apex at the point of obstruction.

An infarct may be *red* or *white.* Virchow regarded the latter as a later stage of the former. Much controversy has taken place on this still debatable question, which, after all, is of trifling importance. Probably the changes which take place in an infarct are somewhat as follows: At the moment of occlusion the artery beyond the embolus contracts, and drives much of the blood out of the infarcted area. The infarct is now, in a sense, white. In course of time the minute collateral channels enlarge, and blood in quantity enters the area in question. Meanwhile the tissues, including the capillaries, having been temporarily deprived of blood, undergo a certain amount of disintegration, and the damaged capillaries

thus allow the inflowing blood to extravasate into the substance of the infarct, which accordingly becomes red. In course of time the vascular engorgement passes off; leucocytes absorb the colouring matter, and the infarct becomes white again. Ultimately the affected area is encapsuled with fibrous tissue and converted into a scar.

Embolism of an end-artery in the brain gives rise to necrosis of the blocked area, followed by 'softening' and liquefaction and the formation of a cyst containing milky fluid.

Infarct of the liver does not occur, because although, as already stated (p. 65), the portal vein is like an end-artery as regards its intrahepatic distribution, and emboli may thus lodge within the liver, these intrahepatic branches connect freely with the hepatic artery through the medium of the capillaries.

Infarction of the heart is generally caused by *thrombosis* in a diseased coronary artery.

Fat Emboli are composed of globules of liquid fat. They are most frequently met with in the arterioles and capillaries of the lungs, generally in connection with injuries of the long bones, especially of those near the epiphyses, the veins in the cancellous tissue of which, being large and patent, allow the liberated marrow cells to enter the circulation and thereby to reach the lungs. Some of the smaller particles may pass through the lungs and lodge in the brain, heart, or kidneys.

Air Emboli may result from wounds about the root of the neck (the 'dangerous area'). The blood-pressure in the large veins entering the thorax being negative, air is sucked into the right heart, and the branches of the pulmonary artery are found full of frothy blood.

It is probable that most of the alleged cases of air embolism are the work of gas-producing bacteria.

The Healing of Wounds.

An Incised Wound.—Blood and lymph escape from the severed vessels. This is followed by coagulation, which glues together the opposing surfaces. The chromocytes disintegrate, their remains being carried away by phagocytes. The now decolorized clot is replaced by

granulation tissue, which consists essentially of fibroblasts and newly-formed blood capillaries.

Fibroblasts.—These are large fusiform cells, having a single ovoid nucleus. Though probably derived from the pre-existing connective-tissue cells, by some authorities their origin is ascribed to the leucocytes and the endothelial cells lining the lymphatics and bloodvessels.

Newly-formed Blood-Capillaries.—Coincident with the appearance of the fibroblasts, certain of the endothelial cells of the neighbouring capillaries throw out projecting buds. These elongate, become hollow, join with other similar buds from adjacent vessels, and so form loops of new capillaries.

In this way the original blood-clot is transformed into the richly vascular *granulation tissue.* Later on the fibroblasts enlarge, develop fibrils in their interior, and thus ultimately form fibrous tissue.

In course of time the newly-formed fibrous tissue contracts and obliterates most of its bloodvessels, a fact which explains the dead-white appearance of the ordinary scar.

It was once thought that primary union—*i.e.*, direct union of divided fibres and cells—took place. It is now known that, in the higher animals at least, this does not occur.

In all forms of wound-healing the process is fundamentally the same—i.e., by means of granulation tissue.

Healing by first intention is said to occur when the sides of an aseptic wound are brought into, and maintained in, apposition.

Lymph is poured out, and, by coagulation, glues together the adjacent surfaces. Granulation tissue forms, and the bloodvessels from the opposite sides anastomose ; organization proceeds in the ordinary way. The epithelium grows over from the edges of the wound and covers it.

Healing by second intention is said to occur when the sides of a wound have not been brought into apposition, or when sepsis has interfered with healing by first intention, or when the parts have been so damaged that suppuration or sloughing has supervened.

As in healing by first intention, lymph is poured out and coagulates. Fibroblasts and new capillaries then appear. The new tissue projects from the base of the wound in the

form of a number of small round red points, or *granulations*, each granulation consisting of loops of capillaries covered on the outside by fibroblasts. The new tissue organizes in its deeper parts, and, *pari passu* with this, fresh granulations form on the raw surface, and in this way the wound heals up from the bottom. Finally, the epithelium grows in from the surrounding margin, and covers the cicatrix, and contraction of the newly-formed fibrous tissue then takes place. Hair and glands are not regenerated.

In the healing of a fractured bone the process is the same as in the healing of soft tissues, with the exception that *osteoblasts* from the periosteum and endosteum take the place of, and subserve the same function as, the fibroblasts, the result being the formation of dense osseous tissue instead of dense fibrous tissue.

The essential part of the cell is the nucleus, and when a portion of the cell-body is severed, the nucleus remaining, it tends to regenerate the part lost.

When a muscle fibre is cut across, the divided ends cannot unite. Such union as takes place between the ends of a divided muscle is effected by fibrous tissue.

The neurone is peculiar in regard to its power of repairing injury (see p. 136).

Repair of Tissue (*e.g.*, Surgical Wounds).

Repair is a mode of growth, not an inflammation.

When a tissue suffers a solution of continuity—*e.g.*, by the surgeon's knife—repair is always (except in the case of regeneration of peripheral nerve fibres) effected by means of *granulation tissue*, which may be defined as embryonic repair tissue. In its earlier stages it consists of small round cells, between which run newly-formed capillaries. Should the tissue have a free surface, as in the case of an open wound, or ulcer, that surface is heaped up into 'granulations,' each of which contains a loop of capillaries. Hence the term 'granulation tissue.' The term 'embryonic repair tissue' is preferable.

The question whether inflammation is a necessary part in the process of repair of wounds—*i.e.*, in the formation of scar tissue—is one of historical interest. Surgeons, noticing that inflammation frequently issued in repair, as in the case of septic wounds, came to regard inflammation as a necessary antecedent to repair. When, however, with the advent of Listerism, it was found that the edges of an aseptic wound, if kept closely together, unite without any of the classical symptoms of inflammation—tumor,

rubor, calor, dolor—and that the healing of wounds is satisfactory precisely in proportion as these symptoms are absent, doubt arose as to whether inflammation is in any way essential to repair. At the present time we may regard it as an accepted canon that aseptic wounds heal without inflammation. The inflammation associated with the repair of wounds is an epiphenomenon resulting from bacterial contamination.

Inflammation may, however, be associated with scar-tissue formation in another way. The essential object of inflammation appears to be the destruction of bacteria. In the effort of destroying them the inflammatory process may or may not result in a solution in the continuity of the tissues. If it does not, there is no need for any reparative process, and no granulation tissue need form; but if it does, a reparative process is necessary, and granulation or repair tissue is produced—*e.g.*, in the tissues round an abscess cavity—which in due course develops into scar tissue.

Sometimes inflammation leads to fibrosis, without causing any antecedent solution of continuity—*e.g.*, in chronic inflammation of the lungs or kidneys. In such cases the fibrous formation may be of service—*e.g.*, in encapsulating a tubercular area; in others it appears to be altogether harmful. By contracting and crushing the parenchyma it certainly is harmful; it is quite possible, however, that it may be largely protective in character.

Granulation or Repair Tissue.—The small round cells met with in newly-formed granulation tissue consist partly of leucocytes and partly of cells descended from fixed cells; notably those belonging to the connective tissue of the part, and to the endothelial lining of the bloodvessels. Under the stimulus which provokes the formation of granulation tissue, be it the cut of the surgeon's knife or a bacterial toxin leading to unmistakable inflammation, these fixed cells tend to divide. Thus, the mature tissue tends to give place to embryonic tissue—in other words, to undergo a preliminary process of *dissolution* in preparation for the process of repair, which is essentially one of *evolution*. The more highly endowed parenchymatous cells, such as neurones and muscle cells, take little part in forming granulation tissue. The nuclei of the neurolemma and sarcolemma may be represented in it, but neither they nor the leucocytes develop into new tissue. *Granulation tissue can only form one kind of tissue —i.e., connective tissue*—and there can be no doubt that its *essential cells are derived from the local connective tissue*. Its bloodvessels are formed by a proliferation of endothelial cells belonging to neighbouring capillaries.

It should be added that some regeneration of epithelial tissue may occur in the process of repair. Thus, the epithelium of the adjoining epidermis may grow over a scar, and some tubular glands appear to possess the power of regenerating their epithelial cells after they have been detached.

Diseases of Scars.

Excessive contraction, causing pain and deformities.
Keloid growth (=hyperplasia of fibrous tissue).
Ulceration.
Epithelioma

Varieties of Fibrosis.

Hyperplasia of connective tissue, or *fibrosis*, occurs under the following conditions:

As Part of a Reparative Process.—When a tissue has suffered a solution of continuity, an embryonic connective tissue (=granulation tissue) forms, and this, by developing into scar tissue, re-establishes the continuity.

Secondarily to Inflammation.—The fibrosis which occurs in this case is not to be regarded as part of the inflammatory process, but as a sequel to, or accompaniment of, it. Examples: The generalized fibrosis which takes place in chronic inflammations—*e.g.*, large white kidney; the formation of adhesions in pleurisy, pericarditis, and peritonitis; the formation of a fibrous capsule round a foreign body, a chronic abscess, or tubercular focus.

Secondarily to Disappearance of the Parenchyma.—Whenever the parenchyma (=epithelial cells, neurones, muscle cells) suffers destruction, hyperplasia of the connective tissue of the part occurs. Thus, in descending lateral sclerosis in the spinal cord, the axons, or nerve fibres, undergo atrophy, and the neuroglia takes on active growth, thus filling up the spaces previously occupied by the axons. Again, in the struggle for existence which always takes place among the several elements of the tissues under conditions of defective nutrition, the hardy connective tissue displays a marked tendency to increase at the expense of the more delicate parenchymatous cells. This is well shown with progressive fibrosis and consequent hardening of the tissues which takes place with advancing years (=senile fibrosis), and in the fibrosis which occurs in passive venous congestion (= brown induration).

It is often difficult to determine how far fibrosis is of this secondary kind and how far it is due to the direct

action of an irritant. This difficulty presents itself in such a malady as granular kidney, for instance. Some hold that even in those cases in which fibrosis manifestly occurs secondarily to atrophy of the parenchyma (*e.g.*, in the symmetrical spinal scleroses), it is produced by irritation—*i.e.*, by the chemical irritation caused by the disintegrating parenchyma.

THE GRANULOMATA.

The term *granuloma* is now becoming obsolete. It embraces the following lesions, which bear a broad, general histological resemblance to one another:

Tubercle.
Syphiloma.
Leprosy.
Glanders.
Actinomycosis.

The characteristic lesion in all these diseases is the presence of a tissue somewhat similar to granulation tissue, developed round a spot at which certain specific parasitic fungi (or their toxins) have lodged.

Tubercle.

When fully developed, an individual or 'anatomical' tubercle consists of:

(*a*) The *giant-celled* or inner zone, composed of one or more large cells, with processes extending outwards between the cells of the next zone. The giant cell contains large nuclei, which are disposed peripherally—often in the form of a crescent. The giant-cells are most abundant in slowly growing tubercles; they are rarely found in rapidly growing ones. They are not distinctive of tubercle, being also found in ordinary granulation tissue, as well as in syphilomata, in leprosy, and in actinomycosis. (The giant cells of sarcoma belong to a different order.)

(*b*) The *endothelioid-celled*, or middle zone, composed of several layers of cells having large and distinctive nuclei.

(*c*) The *lymphoid-celled*, or outer zone, composed of layers of cells identical with lymphocytes.

As regards the bacilli, most of them lie free between the cells, but some are seen lying inside the giant cells, and the endothelioid cells also.

Evolution of the Tubercle.—This is probably somewhat as follows: The tubercle bacilli, having gained entrance into the lymph-stream (*v.* p. 132), ultimately form plugs in certain lymph-capillaries. The latter now constitute so many incubating chambers, in which the bacilli proceed to

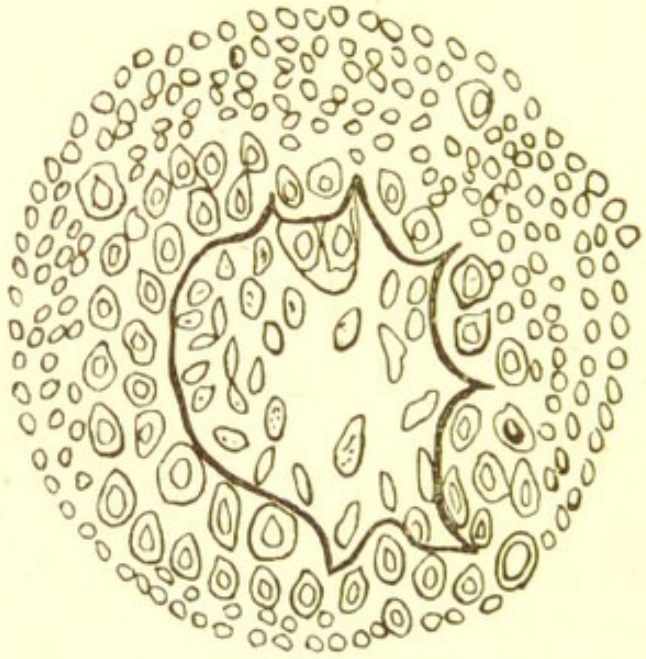

FIG. 8.—DIAGRAM OF AN ANATOMICAL TUBERCLE.

multiply. Some of the bacilli die, and in so doing discharge their special toxins (*v.* p. 48), which by irritant action induce a local tissue reaction. This consists of—

(*a*) Swelling and proliferation both of the endothelial and connective-tissue cells.

(*b*) Subsequently lymphocytes are attracted to the infected area, and form round it a belt, which is probably protective.

(*c*) By the further action of the bacillary toxins the cells at the centre undergo hyaline degeneration, lose their distinctness of outline, and fuse into a homogeneous mass, constituting the 'giant cell.'

A tubercle is non-vascular and tends to caseate. The

bacillary toxins poison the endothelial lining of the adjacent blood-capillaries and thrombosis follows: hence the non-vascularity of the tubercle. Should the patient live sufficiently long, the tubercle undergoes caseation. This degeneration is due to the action of the specific toxin on the cells of a part deprived of its blood supply.

A tubercle never organizes, for, apart from other considerations, no new tissue can organize unless it possesses new blood-capillaries. If the case be a chronic one, a capsule of fibrous tissue forms outside and around the tubercle, as the result of a chronic inflammatory process, which is distinct from the tubercular process proper. This new tissue in course of time contracts upon the tubercle, which finally comes to be represented by a laminated fibrous nodule, in the interior of which a giant cell may or may not be distinguishable.

Neighbouring tubercles may by coalescence form large masses—a condition sometimes found in the cerebellum of children.

Sites.—Let it be clearly understood that tubercles only form in lymphatics. Thus in the case of the lungs they form in the peribronchial, perialveolar, and perivascular lymphatics.

The favourite sites for tubercles are: the tonsils, the lymphatic glands, the lungs, the synovial membrane of joints, the pleuræ, the peritoneum, the pia mater of the brain, the epididymis, the Fallopian tubes, and the cancellous tissue of bones. Should the tubercle formation be active, and much toxin be discharged into the general circulation, there result—

Fever (hectic);
Emaciation;
Fatty degeneration (liver and heart);

and a tendency to

Amyloid degeneration (*v.* p. 10).

Acute Miliary Tuberculosis.—A deposit of tubercle—as, for example, in the bronchial glands, or in the apex of the lung—may at any time light up a general

infection of the system. The tubercle bacilli in these cases are probably distributed by the blood-stream (by erosion through the walls of a bloodvessel or thoracic duct), subsequently passing through the thin capillary walls into the lymph-stream. When this happens the condition is known as *acute miliary tuberculosis*, of which there are three main types: that affecting the lungs, that affecting the pia mater of the brain, and that affecting the peritoneum and abdominal viscera. Not infrequently all three are combined.

Bovine and Human Tuberculosis.—The long-debated question as to whether tuberculosis is or is not transmissible from the animal to the human being is answered emphatically in the affirmative, so far as the bovine animal is concerned, in the second interim Report of the Royal Commission on Human and Animal Tuberculosis, issued February 1, 1907.

The following are the conclusions arrived at. It will be seen that the Commissioners are equally emphatic in urging that the utmost care should be exercised in regard to the supply of milk.

'There can be no doubt but that in a certain number of cases the tuberculosis occurring in the human subject, especially in children, is the direct result of the introduction into the human body of the bacillus of bovine tuberculosis; and there also can be no doubt that in the majority at least of these cases the bacillus is introduced through cow's milk. Cow's milk containing bovine tubercle bacilli is clearly a cause of tuberculosis, and of fatal tuberculosis, in man.

'The facts indicate that a very large proportion of tuberculosis contracted by ingestion is due to tubercle bacilli of bovine source.

'A very considerable amount of disease and loss of life, especially among the young, must be attributed to the consumption of cow's milk containing tubercle bacilli. The presence of tubercle bacilli in cow's milk can be detected, though with some difficulty, if the proper means be adopted, and such milk ought never to be used as food.

'There is far less difficulty in recognizing clinically that a cow is distinctly suffering from tuberculosis, in which case she may be yielding tuberculous milk. The milk coming from such a cow ought not to form part of human food, and, indeed, ought not to be used as food at all.

'Our results clearly point to the necessity of measures more stringent than those at present enforced being taken to prevent the sale or the consumption of such milk.'

These conclusions are in distinct conflict with the views held by the late Dr. Koch, who, in a paper read before the British Congress on Tuberculosis in London on July 23, 1901, reaffirmed his belief that the disease was not transmissible from animals to man. In fact, the Royal Commission was to all intents and purposes called into existence by that pronouncement, for it was appointed on August 31 in the same year.

The Commissioners selected were Sir Michael Foster, F.R.S.; Professor Sims Woodhead (Cambridge); Professor Sidney Martin, F.R.S. (University College, London); Professor MacFadyean (Principal, Royal Veterinary College, London); and Professor Boyce (University College, Liverpool).

Lupus.

Lupus is chronic tuberculosis of the skin (cutis vera) and mucous membranes. Typical tubercles are present, but the bacilli are few and very difficult to find. The common situation of lupus is about the nose and cheeks, but it may also occur on the trunk and limbs. When it involves the mucous membranes it generally does so by extension from the skin.

The disease rarely begins after the age of twenty-five, but it may *recur* at any age.

Syphilis.

For a full account of the lesions found in syphilis, see p. 175.

Leprosy.

Leprosy is characterized by the formation of granulomata arising in connection with the presence of the *Bacillus lepræ*.

The granuloma is composed principally of endothelioid cells, with occasional giant cells, and may occur either in the form of (1) distinct nodules, or (2) as a diffuse infiltration.

The tissue tends to degenerate, being either absorbed or leaving a cicatrix. There is *no caseation as in tubercle*.

Sites. — Skin, mucous membranes, nerves, testicles, liver, and spleen.

Glanders.

Glanders is a highly contagious disease due to the *Bacillus mallei*, and attacking primarily horses, mules, and asses, but also communicable to man from the diseased animal.

In the horse two varieties are recognized—glanders proper and farcy—each of which may occur in the same animal at the same time. The lesion is a granuloma, the cells of which are almost entirely composed of polymorphonuclear leucocytes, between which are the specific bacilli; no giant cells are present. In course of time necrosis takes place. Glanders proper begins (in the horse) in the septum nasi and neighbouring parts; the lymphatic glands of the neck and thorax soon become affected, and subsequently the lungs, liver, and spleen.

In the variety known as farcy the infection takes place through the skin, the disease then beginning in the superficial lymphatic vessels and glands. Secondary nodules form in internal organs, as in glanders proper.

In man the disease occurs chiefly in grooms, knackers, and those who work amongst horses, infection taking place through an abrasion of the skin, or through the mucous membranes of the mouth, nose, or eyes. The symptoms may be either acute or chronic, while, as in tuberculosis, a chronic attack may at any time take on the characters of the acute form and rapidly prove fatal.

Actinomycosis.

Actinomycosis is a disease usually of cattle (oxen), occasionally of man, and is due to the growth of the actinomyces, or ray-fungus. It is probably seldom transmitted directly from one animal to another. The fungus is common on such cereals as barley, and a man may be inoculated by chewing the raw grain or by inhaling the fungus during threshing, etc.

The granuloma is at first composed principally of lymphocytes, polymorphonuclear leucocytes then appear, and giant cells are not infrequent. In the central part are clumps of the ray-fungus.

Around the granuloma there is often considerable fibrous thickening, and thus the condition may be mistaken for a sarcoma. In course of time softening, suppuration, and sinus-formation occur. The pus is characteristic: it may be serous or viscid, and in either case contains the golden-yellow colonies of the parasites.

In man the common sites are the face, mouth, jaws, and neck. The infection may spread to the mediastinum. The intestines may also be attacked, and from them the disease may spread to the mesenteric glands, peritoneum, and liver. The lungs may be a primary seat of infection, as in threshers.

TUMOURS (NEOPLASMS).

A tumour is a local overgrowth, forming a lump of new tissue, more or less sharply demarcated from the normal tissue around, and subserving no function useful to the organism. It is outside the control of the central nervous system.

This definition includes the granulomata among the tumours, though these are not generally regarded as such.

Classification of Tumours.

- **Innocent**
  - Mesoblastic
    - Connective-tissue growths
      - Myxoma.
      - Fibroma.
      - Papilloma.
      - Glioma.
      - Chondroma.
      - Osteoma.
      - Odontome.
      - Neuroma.
    - Myoma.
    - Angioma.
    - Lymphangioma.
  - Epiblastic adenoma.
  - Hypoblastic adenoma.
  - [Cysts.]
  - [Teratomata.]
- **Malignant**
  - Mesoblastic
    - Sarcoma.
    - (Endothelioma ?).
  - Epiblastic
    - Squamous epithelioma
    - Rodent ulcer
    - Spheroidal cancer
    - Duct cancer

    (The carcinomata.)
  - Hypoblastic: Columnar epithelioma (The carcinomata.)
  - [Colloid.]
  - [Melanotic.]

The Innocent Tumours.

An *innocent tumour* is one consisting of a tissue, for the most part normal in type, resembling more or less completely the tissue of the part from which it grows. Its growth is generally slow; it is usually circumscribed and encapsuled; it does not recur after removal nor reproduce itself in distant parts.

The Pathology of the Innocent Tumours.—It is probable that some innocent tumours (*e.g.*, adenomata, myomata, lipomata) are traceable to embryonic remains which have in some way been stimulated into activity. Local irritation, such as from discharges or friction, may give rise to polypi and papillomata. Some innocent growths, such as certain warts and molluscum contagiosum, are apparently of parasitic origin.

The pathology of the cysts and the teratomata is considered under their individual headings.

Degeneration.—

A **Myxoma** is composed of stellate connective-tissue cells, which by the union of their processes form a delicate network, within the meshes of which is a clear mucoid material containing a small number of round cells. The tumour thus resembles in structure the tissue which preforms all the connective tissues of the fœtus, also the vitreous humour of the eye and the Whartonian jelly of the umbilical cord.

Sites.—The subcutaneous tissues, bladder, rectum, nerves, and spinal cord. A myxoma may also occur in association with cartilaginous tumours of the parotid and the testicle, and sometimes in connection with sarcomata. (The so-called 'mucous' polypus of the nose is probably a mass of hypertrophied and œdematous mucous membrane.)

A **Fibroma** is a tumour composed of connective-tissue cells and white fibres arranged in wavy bundles. It is round or lobulated in form, and generally enclosed in a distinct capsule. On section, and viewed obliquely, it looks like 'watered silk.'

Fibromata may be *hard* or *soft*, according as the elements composing them are loosely or closely packed.

Sites.—The hard fibroma is met with on the gums (fibrous epulis); the soft fibroma, in the skin, as a pedunculated mass (molluscum fibrosum). Other situations are: Fasciæ, tendon sheaths, periosteum, base of skull, nerves, and uterus.

Most so-called *neuromata* are in reality fibromata involving nerve trunks.

A **Papilloma** (sometimes classed as an epithelial tumour) consists of a main stalk of connective tissue,

giving off primary and sometimes secondary processes, the whole being capped by the normal epithelium of the part. This, however, *never invades the underlying tissue* (thus differing from carcinoma).

The connective tissue of papillomata is more cellular than normal connective tissue, being sometimes even myxomatous, and the bloodvessels are more dilated. In certain situations—*e.g.*, the bladder—papillomata are prone to bleed.

Sites.—The skin (warts), larynx, rectum, bladder.

A **Glioma** is a tumour growing from the delicate connective tissue (*neuroglia*) of the nervous system, and not sharply demarcated from the surrounding parts. It is soft and translucent, not unlike the grey matter of the brain.

Structurally it consists of a large number of closely packed stellate cells, with numerous branching processes, which interlace to form a network. It is often very vascular, and its vessels, having thin walls, are liable to rupture; hence *the frequency of hæmorrhages within it.* It is non-malignant, and dangerous only on account of the pressure it exerts (*v.* Glio-sarcoma, p. 93).

Sites.—Brain, spinal cord.

The so-called *glioma of the retina* contains, among other cells, some which resemble epithelium, and for this reason the growth is sometimes classed among the epithelial tumours. It is liable to extend along the optic nerve and to recur after removal. It occurs most frequently in young children.

A **Lipoma** is composed of ordinary adipose tissue. It is the commonest of all the tumours in man, and may attain to an enormous size (60 pounds). It may be either *circumscribed* or *diffuse.*

A *Circumscribed Lipoma* (the usual kind) is a rounded, lobulated tumour of elastic or doughy consistency, contained within a distinct capsule. It is generally single, but two, ten, or more may coexist.

Sites.—The common situation is in the subcutaneous tissues, but it may occur in the subserous tissues (*e.g.*, of peritoneum, pleura), in the subsynovial and submucous tissues, between or in muscles, in the periosteum, and in the meninges of the brain and spinal cord.

A *Diffuse Lipoma* is a diffuse symmetrical overgrowth of subcutaneous adipose tissue, not encapsuled, generally occurring beneath the chin or at the back of the neck. It is said to be most frequently met with in beer-drinkers.

A lipoma may contain other tissues besides fatty. Examples of such are myxo-lipoma, fibro-lipoma, nævo-lipoma.

Xanthoma.—This is a modified form of lipoma, its substance resembling embryonic fatty tissue, with an admixture of small round cells. It occurs on the eyelids in the form of flat elevations of a yellow colour. It may also be found in diabetes (but rarely on the eyelids or face).

A **Chondroma** is a tumour composed mainly of hyaline cartilage, though it may also contain a certain amount of fibro-cartilage. It may consist either of a single mass of cartilage, or be composed of lobules bound together by a vascular fibrous tissue. Ossification and calcification are exceptional.

Sites.—The most common situation of chondromata is the interior of the phalanges of the hand, where they are often multiple, forming rounded knobs, which may attain the size of walnuts. They are only found in the bones which develop from cartilage. They probably originate either from misplaced islets of cartilage or from the epiphyseal cartilage.

Chondromata also occur in the *parotid gland* (where they probably originate from Meckel's cartilage) and in the *testis;* but in these situations the tumour is generally associated either with myxomatous or sarcomatous elements (or with both). Pure chondroma of the testis is exceedingly rare.

An **Osteoma** is a tumour composed of bone tissue. There are two chief varieties: (*a*) Cancellous, or spongy; and (*b*) compact, or ivory.

(*a*) *Cancellous.*—This is usually met with as a pedunculated, 'cauliflower' mass of about the size of a walnut, growing near the extremity of a long bone.

It appears to originate from the epiphyseal cartilage, and consists of a mass of spongy bone limited by a shell of compact bone. During its growth the tumour is encased in a thin layer of continually growing hyaline

cartilage, and it is by the ossification of this that it increases in size. When the epiphysis becomes united to the diaphysis, growth ceases, and the tumour remains stationary. The affected bone, as a rule, loses in length what it gains in 'new growth.'

Sites.—Lower end of femur, ungual phalanx of great toe, upper ends of tibia and humerus. Sometimes the tumours are multiple and hereditary.

(*b*) *Ivory.*—This is composed of very dense bony tissue, of the consistence of ivory. It is rounded in form, and usually sessile.

Sites.—Although a tumour of this variety may develop in any bone, its most frequent sites are: Frontal sinus, orbit, external auditory canal, angle of the lower jaw, mastoid process, ilium, and scapula.

Odontomes (Tooth Tumours).—'Odontomes are tumours composed of *dental tissues* in varying proportions and different degrees of development, arising from teeth germs or teeth still in the progress of growth' (Bland-Sutton).

The two most important are—

(*a*) Epithelial odontomes.
(*b*) Follicular odontomes.

(*a*) *Epithelial Odontomes* (*Multilocular Cystic Tumours*) are composed of a number of small cysts lined by cubical epithelium, and embedded in a fibrous stroma. They contain a viscid fluid, and appear to originate in branching columns of epithelial cells derived from the enamel organ, which cells break down in their more central parts. The jaw becomes expanded, but growth is slow. These cysts are non-malignant, showing no tendency to affect the glands or to disseminate.

(*b*) *Follicular Odontomes* (='dentiferous cysts') are cysts which form in connection with misplaced and non-erupted teeth. The expanded dental sac represents the cyst wall. The interior contains a viscid fluid and the crown of the non-erupted tooth, the fang of which is usually fixed to the cyst wall, though sometimes the tooth is loose. With rare exceptions, follicular odontomes form only in connection with the *permanent* teeth, and more particularly with the canine of the upper jaw. The tumour grows slowly. Owing to expansion of the surrounding bone, 'egg-shell crackling' may in course of time be felt on pressure. (These cysts must be distinguished from 'dental cysts' which develop from the fangs of normally erupted teeth.)

A **Neuroma** is composed of nerve cells, and is extremely rare. Cases have been described as occurring in the skin of children and in the sympathetic ganglia.

(A 'false' neuroma is a fibroma growing from the sheath of a nerve; an 'amputation' neuroma is merely a mass of fibrous tissue on the cut end of a nerve.)

A **Myoma** is a tumour composed of muscle tissue. Two varieties occur: the (*a*) rhabdomyoma, consisting of striated muscle; and the (*b*) leiomyoma, consisting of non-striated muscle.

The *Rhabdomyoma* is very uncommon, and usually congenital. Its usual seat is the kidney, where it probably arises from inclusion of some of the fibres of the lumbar muscles during fœtal development. The component elements rarely present the characteristics of normal striated muscle, but consist chiefly of spindle-shaped cells, together with a large number of embryonic cells and only a few striated fibres.

The *Leiomyoma* only develops *from pre-existing unstriated muscle fibre*, and occurs most commonly as the 'uterine fibroid'; but it occasionally occurs in the œsophagus, stomach, intestines, and prostate. It has also been found in connection with the broad ligaments and the ovaries.

When occurring in the uterus, this tumour is composed of bundles of spindle-shaped unstriated muscle fibres, which interlace in various directions. In places the fibres are arranged concentrically, presenting the appearance of tiny balls of cotton. There is generally a fair amount of fibrous tissue present, so that the tumour is often called a *fibro-myoma*.

The **Angiomata** are tumours composed of dilated bloodvessels. They are of three kinds—

Simple nævus.
Cavernous nævus.
Plexiform angioma.

A *Simple Nævus* consists of a mass of dilated capillaries and venules held together by connective tissue. It is nearly always congenital, and usually tends to increase in size for a few months after birth.

A *Cavernous Nævus* resembles in structure the corpus cavernosum of the penis, and consists of a series of intercommunicating spaces, the walls of which are formed

of a fibrous stroma lined by endothelium. Small arteries open directly into these spaces, and veins carry the blood away.

The tumour may be provided with a distinct capsule, or it may merge gradually into the surrounding tissue.

It may be congenital, but more frequently it develops in later life.

Sites.—Skin of face, trunk, limbs, and liver.

Plexiform Angioma.—When a single artery becomes dilated, thinned, elongated, and tortuous—resembling a varicose vein—the condition is known as *arterial varix.* When the same condition affects several neighbouring arteries, it is known as *cirsoid aneurism.* Deficiency in the muscular and elastic elements in the walls of the affected arteries would suffice to induce the condition. If the dilatation involves the capillaries and veins as well, with the formation of a pulsating, bluish, spongy tumour, the condition is termed *plexiform angioma.*

Sites.—May be found on any part of the body, the usual seat being the scalp, where it affects the temporal, posterior auricular, and occipital arteries.

A **Lymphangioma** is a tumour composed of dilated lymphatics, associated with fibrous hyperplasia of their walls and atrophy of the intervening tissue. The dilatations may be so extreme as to constitute actual cysts. Three kinds are described—(i.) *Lymphatic nævus* (occurring in the skin and tongue); (ii.) *cavernous lymphangioma;* (iii.) *lymphatic cyst* (occurring in the neck as cystic hygroma and hydrocele, axilla, chest wall, and always congenital).

The **Adenomata** are tumours consisting of normal gland tissue (thus differing from the carcinomata, which consist of a perverted type of gland tissue) arising in connection with, and constructed on the model of, the secreting gland from which they grow, but their ducts do not enter those of the gland, and they contribute nothing to its normal functions.

Imitating the structure of the gland from which it springs, an adenoma consists, when growing from a compound tubular gland, of acini and ducts, and, when growing from a simple tubular gland, of tubules. The acini and tubules alike are lined by regular epithelium *which*

does not infiltrate into, but is sharply demarcated from, the surrounding tissue.

The connective-tissue stroma varies in amount. In some cases it is so considerable that the growth is called an *adeno-fibroma.* In the quickly-growing forms myxomatous and sarcomatous elements may be intermingled with the stroma. Such mixed forms are known as *myxo-adenoma*, *sarco-adenoma*, etc. Further, the tubes and acini may become distended into cysts forming a *cysto-adenoma*, and occasionally the stroma may project into the lumen of the acini, when the growth is known as a *papillary adenoma.*

Adenomata are generally encapsuled, and not infrequently multiple. They never reproduce themselves in distant organs.

Sites.—Mamma, thyroid, ovary, intestines, and prostate.

Cysts.

A cyst is a closed sac of abnormal development, the contents of which are fluid or semi-fluid.

The different varieties are—

Retention Cysts constitute the majority of cysts ; they are caused by obstruction to the outflow from a gland or cavity. Mucous, sebaceous, mammary, renal, pancreatic cysts, and ranula, are examples. They are lined by a layer of epithelium.

Cysts formed by the Dilatation of a Fœtal Tube which Normally is obliterated—e.g., parovarian cysts, cysts in connection with the thyroglossal duct, urachus, Wolffian duct, and Müllerian duct.

Cysts containing an Animal Parasite—e.g., hydatid.

Distension Cysts, resulting from hernial protrusions of the synovial membrane of a joint, and hernial protrusions of tendon sheaths (ganglion). Also cysts of the thyroid.

Neural Cysts, of which meningocele and spina-bifida are examples.

Cysts resulting from Degeneration in the Central Part of a Tumour—e.g., in sarcomata.

Blood Cysts. These are due to extravasated blood

becoming encapsuled, or to hæmorrhage occurring into any ordinary cysts.

Lymphatic Cysts (see Lymphangioma, p. 83).

Implantation Cysts are caused by the implantation of the epidermis, conjunctiva, or other mucous membrane, into the deeper tissues, after such an injury as a stab with a hatpin, fork, etc. In its new situation the epithelial cells proliferate and form a cyst.

Teratomata.

The term *teratomata* (*teras*, a monster) is applied to tumours composed of an assortment of many different tissues mixed in varying proportions. Some contain dermal structures—*e.g.*, skin, nails, hair, and teeth (=dermoid cyst), and others may contain muscle, cartilage, bone, nerve, viscera, or, indeed, any tissue of the body. They appear to result from the inclusion of a germ cell within the tissues of an embryo.

Dermoid Cysts occur most commonly in the ovaries, but also in the testicles, about the angles of the orbit, in the neck, and elsewhere. The cyst wall is composed of skin, and inside the cyst are hair, nails, or teeth, and sebaceous matter. In many cases they seem to result from inclusion of the epiblast during the closure of the embryonic clefts. In the case of the ovary, they probably either develop from the Wolffian body—an epiblastic structure—or result from the aborted growth of an ovum.

The Malignant Tumours.

A *malignant* tumour is one consisting of a perverted type of tissue—differing, *i.e.*, from any normal tissue ; it generally exhibits extreme activity of growth, increasing in size until the fatal end ; it tends to invade the surrounding tissues irregularly, so that there is no sharp division between it and them ; encapsulation being exceptional, it tends to produce itself in distant parts.

There are two chief kinds—the *sarcomata*, in which the characteristic 'malignant' cell belongs to the connective-tissue type, and the *carcinomata* in which the malignant cell belongs to the epithelial type.

The Pathology of Malignant Disease.—Perhaps the greatest problem confronting the pathologist is the nature and causation of malignant disease.

Certain factors in causation are definitely known. A

blow may determine the occurrence in the injured region of malignant disease, either sarcoma or carcinoma, just as it may determine the occurrence of a granuloma (*e.g.*, gumma or tubercle). Chronic local irritation is a common exciting cause of malignant disease.

A diseased tooth may induce sarcoma; carcinoma of the alimentary tract occurs most frequently in those parts which are most subjected to irritation—*e.g.*, the lower lip, the tongue, the œsophagus (at its beginning and end, and where it is crossed by the left bronchus), the pyloric orifice of the stomach, the large intestine, especially at the flexures (the liability increasing from cæcum to rectum—*i.e.*, with the increasing hardness of the fæces, while, on the other hand, cancer of the small intestines is rarely met with, the contents being fluid). Witness, again, the occurrence of chimney-sweep's cancer in the scrotum, and the frequency of cancer in the cervix uteri. 'Out of 1,876 cases of carcinoma of the cervix uteri investigated at the Middlesex Hospital Research Laboratories, no less than 1,796 had been married. Of these, only 9 per cent. had not borne children. Clinically, a case in an undoubted virgin was almost unknown. The reason of this remarkable relationship between the disease and sexual life was found by pathology to be due to the fact that every case of carcinoma of the cervix appeared to be founded on a chronic cervicitis' (Bonney). Fournier says that epithelioma of the tongue is rarely found except in those who have syphilitic leucoplakia, and who at the same time smoke in excess. Few syphilitics, however, who do not smoke ever develop lingual cancer, and still fewer cases of this disease are found in smokers who are non-syphilitic.

The irritation, in many cases at least, would appear to act by inducing a chronic inflammation, and some clinicians have spoken of a 'precancerous inflammatory' phase.

It should be observed that the various forms of local irritation mentioned merely act by preparing the soil. Once the malignant process is started, it goes on independently of such irritation.

There is an undoubted relation between the condition of the blood and the liability to malignant disease. This is especially noticeable in the case of carcinoma, which may sometimes be observed to take on phases of quiescence or activity, which probably stand in causal relation to parallel changes in the blood. It is also probable that the increasing liability to carcinoma after middle life is in large measure associated with the condition of the blood.

Some of the salient facts in the pathology of malignant disease will now be considered:

(*a*) The rapid multiplication and survival, at the expense of the normal tissues, of the 'malignant' cells (*epithelial* cells in the case of the carcinomata, embryonic *connective-tissue* cells in the case of the sarcomata). It is by virtue of this rapid multiplication, and the ability of the new-born cells to shift for themselves, to secure the conditions needful for their survival, that the invasion of the healthy tissue (= infiltration) at the confines of the tumour takes place. The multiplication of the malignant cells is associated with the development of new bloodvessels; this cellular activity is much greater than in the case of the granulomata.

(*b*) The 'looseness' of the malignant cells. The rapidly multiplying malignant cells are not, like the fixed cells of a normal tissue, securely held in place. On the contrary, they are more or less loose, and are thus liable to be conveyed to distant parts. Such loose cells can either pass straight into the lymphatics, which are continuous with the intercellular spaces throughout the body, or they may enter the blood-stream through the walls of imperfectly-formed bloodvessels.

(*c*) The breeding true of the secondary growths. These always reproduce the same type of cell as that belonging to the parent tumour: a squamous epithelioma of the tongue produces a similar growth in the local lymphatic glands, which normally contain no epithelial cells; carcinoma of the rectum, containing the characteristic columnar cells of the part, gives rise to secondary growths displaying the same type of cell, whether they form in the liver, inside the shaft of a long bone, or elsewhere; a melanotic sarcoma of the skin or the eye reproduces itself as a melanotic sarcoma of the lungs or liver.

(*d*) The transference of the characteristic malignant cells to secondary sites. This is rendered possible by the looseness of the cells. That the transference occurs is shown by the fact that the tumour breeds true.

(*e*) The fact that the transferred malignant cells can survive and multiply in the secondary site, giving rise to a tissue similar to that of the primary tumour. It is very doubtful if a cell of a normal tissue—say the liver—even if it became detached and conveyed to a distant tissue, could survive in its new habitat, much less multiply and form new tissue. The ability of malignant cells to multiply in distant tissues is on a par with its ability to multiply in the tissues immediately surrounding a malignant tumour.

(*f*) The multiplication of malignant cells is associated with an irritant action on the normal cells of the part. These are apt to break up and become absorbed. In the case of the carcinoma, well-marked hyperplasia of the connective tissue occurs. Evidently there are developed in connection with the

malignant cells, irritant substances, and it seems probable that by the disturbing action which these exert on the normal cells of the part, the survival of the malignant cells is secured; otherwise it is doubtful whether they could survive in the struggle for existence with the normal cells.

(*g*) The fact that malignant tissue is a morbid tissue, nowhere normally met with in the body; that of the sarcomata is a permanently embryonic form of connective tissue; that of the carcinomata a perverted type of glandular tissue.

(*h*) The tendency for malignant tissue to degenerate.

(*i*) The tendency for malignant tissue to be invaded by bacteria. 'Owing, no doubt, to that defective resistance which seems to be a feature of all neoplastic tissues, cancer, very early in its history, long before it has burrowed its way to the surface, becomes the seat of a staphylococcus infection—an infection by the so-called *Micrococcus neoformans* of Doyen. And there is reason to believe that much of the pain and swelling and inflammation in connection with the tumour, and much, if not all, of the so-called cancerous cachexia, is due to this micro-organism' (Sir A. E. Wright, *Lancet*, September 17, 1910).

So far as the above statements are concerned, we are on fairly certain ground concerning the pathology of malignant disease. How far do they give us an insight into the real nature of the malignant process? It is obvious that the crux of the problem of malignancy is how to explain the abundant multiplication and survival of the malignant cells. It is noteworthy that the only fixed cells of the body which normally are capable of multiplying are just the very cells which constitute 'malignant' cells—epithelial cells, connective-tissue cells, and endothelial cells. What we have to ask is how these cells came to multiply so extravagantly as they do in malignant disease, and how they are able to survive at the expense of the normal tissue. Their rapid multiplication can only be due to one of two causes: either (*a*) to some cell, or a few cells, spontaneously becoming endowed with unwonted reproductive activity, and so giving rise to colonies of malignant cells (we can conceive that a cell, or a limited number of cells, might, under special influences, throw back to some remote phylogenetic ancestor, and dissociating themselves from the vast cell community of which they form part, assume the rôle of rebels, which would virtually constitute parasites); or (*b*) to the action of some irritant constantly lashing the malignant cells into inordinate reproductive activity. The kind of irrita-

tion which sometimes initiates malignancy would not suffice ; we should need to postulate a *continuous irritant acting on each individual cell* in the growing portions of both the primary and secondary tumours. Some observers (Jackson Clarke, and others) claim to have discovered protozoa in the cells both of carcinoma and sarcoma. Their findings are not generally accepted. If these were substantiated, the mystery of malignant disease would be cleared up. Certain it is that many of the phenomena of malignant disease can be explained on the parasitic theory. Thus : local irritation, by lowering vitality, diminishes resistance to parasitic invasion ; the parasites provide a lasting irritant (probably of a chemical nature). Under this continued specific irritation the malignant cells undergo a ceaseless multiplication, producing a degraded type of tissue, containing loose cells, and displaying a liability to degenerate ; the loose cells are carried away with the parasites to the secondary sites, and, being thus subjected to the same kind of irritation as in the primary growth, behave in the same way ; the chemical irritation caused by the parasites so disturbs the nutrition of the normal tissues that the malignant cells are able to survive in the struggle for existence with the normal cells.

A question of interest in this connection is whether, as Bashford maintains, all the malignant cells of the primary growth—say, carcinoma of the tongue—are derived from one primary cell (or a few primary cells), or whether the normal cells of the tissues immediately surrounding the tumour also multiply and furnish their quota of malignant cells. The definite establishment of the former view would strongly militate against the parasitic theory.

Sarcomata.

A sarcoma is a malignant tumour growing from connective tissue, and composed of *embryonic* connective tissue.

Broadly speaking, the more embryonic the cells, the more malignant is the tumour.

Structure.—The varieties of sarcoma represent stages in the ordinary development of connective tissue—from the round cell to the spindle cell, but stopping short of fully-formed connective tissue.

Intercellular substance is always present, but though very evident in some cases, it is difficult to distinguish in others. It may be fluid and homogeneous, granular or finely fibrillated, and sometimes cartilaginous or osseous.

The bloodvessels are usually very numerous, and generally embryonic in structure. Often they are mere channels or spaces between the cells of the tumour. This explains the frequent occurrence of hæmorrhage into the substance of the growth; also the way in which the specific cells of the tumour can be carried into the circulation and deposited in distant organs, there to set up secondary growths.

A sarcoma in some cases appears to be circumscribed by a capsule, but this is merely a condensation of the surrounding tissues, and is generally infiltrated with the sarcoma cells.

Mode of Spreading.—Sarcomata spread locally by *infiltrating* the surrounding tissues. At the growing border of the tumour there is a great excess of small round cells; these advance in all directions, absorbing the normal tissues (muscles, glands, etc.) in the immediate vicinity.

The most common channel of dissemination in distant parts is the *blood-stream:* detached groups of the cells pass into the circulation, and are carried by the veins into distant organs (notably the lungs), there reproducing the structure of the original growth.

They may also spread by the lymphatics: this happens in the case of melanotic sarcoma, sarcomata of lymph glands, tonsil, thyroid, testis, as likewise all quickly growing sarcomata.

The classification of the sarcomata is based upon the prevailing type of constituent cell:

Ordinary Forms.	*Special Forms.*
Small round-celled.	Lympho-sarcoma.
Large round-celled.	Myeloid.
Small spindle-celled.	Alveolar.
Large spindle-celled.	Melanotic.
	Myxo-sarcoma.
	Chondro-sarcoma.
	Osteo-sarcoma.
	Glio-sarcoma.

Small Round-celled Sarcomata are the commonest form of sarcoma, and, next to the melanotic, the most malignant. They grow rapidly, infiltrating the surrounding tissues, often attaining a great size, and disseminate through the bloodvessels. They are encephaloid in appearance, being to the naked eye very like the encephaloid carcinoma.

Sites.—They may occur in any organ: in the bones, glands (especially the mamma and testis, muscles, and subcutaneous tissues).

Large Round-celled Sarcomata are rarer and less malignant than the last-named variety. The cells are large, and have a round and distinct nucleus.

Spindle-celled Sarcomata consist of oat-shaped or fusiform cells, tapering to a point, which often bifurcates. They are arranged in bundles, which take different directions, so that in section under the microscope some of them appear rounded and others spindle-shaped.

They are firmer than the round-celled sarcomata, and they may contain an admixture of myxomatous tissue (*myxo-sarcoma*), cartilage (*chondro-sarcoma*), and bone (*osteo-sarcoma*). In slow-growing forms some of the spindles may be converted into fibrous tissue (*fibro-sarcoma*).

Sites.—Bones, subcutaneous tissues, fasciæ.

The **Lympho-Sarcomata** are composed of cells identical with those of the round-celled sarcomata, and they contain a delicate, fibrillated, intercellular substance.

Sites.—Their common seat is in the bronchial and mediastinal lymphatic glands, but they are also found in the mesenteric and other lymphatic glands.

The tumours found in *chloroma* (*v.* p. 31) are probably lympho-sarcomata.

Myeloid Sarcomata grow from the marrow of certain bones.

In appearance the cut surface often suggests a piece of liver, owing to the presence of extravasated blood which has undergone pigmentary changes. Cysts are common.

The cells composing this tumour are of two kinds—(*a*) *spindle cells*, which form the bulk of the growth, and (*b*) *multinuclear giant cells*, scattered throughout.

The *giant cells* are large, irregularly spheroidal, and

generally without processes ; their *nuclei are scattered throughout the cell contents*, not concentrated at the periphery, as in the giant cells of tubercle.

The tumour is often *very vascular*, so that it may pulsate, and thus be mistaken for an aneurism. Secondary growths are exceedingly rare, so much so that some pathologists would assign to these tumours a separate class—the myelomata.

Sites.—The lower end of femur, upper end of tibia, upper end of humerus, and the lower jaw.

Alveolar Sarcomata, which are very rare, grow from the skin. Their round or oval cells are grouped in alveoli formed by fibrous tissue. Between the cells is a delicate, fibrillated, intercellular substance.

Melanotic Sarcomata contain an *intracellular* pigment (melanin), elaborated by the cells themselves and differing in composition from the ordinary blood-pigments in containing sulphur, but usually no iron. An iron-containing pigment may, however, sometimes be found *between* the cells as the result of blood extravasation. They vary in colour from a sooty brown to an intense black.

Some of the cells are spindle-shaped and others epithelioid, and they are sometimes contained in alveoli, as in the alveolar sarcoma. When a melanotic sarcoma grows from the skin, the alveolar structure with epithelioid cells is the rule, and accordingly some pathologists regard this form as a carcinoma.

Although *locally* far less malignant than many other kinds of sarcomata, the melanotic sarcomata are the most malignant of all tumours, on account of their rapid dissemination. Thus, by the time the primary growth has reached the size of a filbert, secondary growths are generally to be found in the lungs, liver, kidneys, and brain. *They disseminate by the lymphatics as well as by the bloodvessels.*

They are very rare, about one case being seen at a large London hospital each year.

Sites. —The primary seats are the tissues which normally contain pigment—*i.e.*, the skin and the uveal tract of the eye (iris and choroid).

The **Osteo-Sarcomata**, as primary growths, are met

with almost exclusively in bone. As a rule, *calcification* is more common in them than true ossification, but spicules of true bone can generally be detected.

The **Glio-Sarcomata** grow from the neuroglia of the nervous system, and are composed of embryonic neuroglia. They are the commonest of all forms of cerebral tumours.

Endotheliomata.

The **Endotheliomata** are tumours growing from the *endothelium* of serous membranes (pleura, peritoneum, meninges of brain, synovial membrane of joints and tendon-sheaths), lymphatics, bloodvessels, and sometimes from the endothelium in the parotid gland, testicle, and ovary. (Such tumours growing from serous membranes are sometimes called *Mesotheliomata*, and when growing from the perivascular lymphatics, *Peritheliomata*.) The cells are large, round, and sometimes 'epithelioid' in shape, with no intercellular substance, and they are contained in alveoli formed by fibrous tissue. The structure of the endotheliomata thus resembles that of the carcinomata.

The endotheliomata, as a rule, develop very slowly; they are only occasionally malignant, secondary growths and recurrence after removal being rare.

Psammomata are endotheliomata which grow from the pia mater of the brain and the choroid plexuses. The cells are arranged in groups lying in a fibrous stroma. Each group of cells is composed of concentric layers, in the centre of which is a calcified sandlike particle due to the degeneration of the most central cells. In the brain a psammoma rarely exceeds the size of a shelled walnut.

The Carcinomata.

A *Carcinoma* is a malignant tumour growing from, and containing as its essential elements, epithelial cells (epiblastic and hypoblastic). It may be defined as a *malignant tumour consisting of perverted gland tissue*.

The epithelial cells—which constitute the malignant cells proper—manifest extraordinary powers of multiplication and survival, thriving at the expense of the normal tissues. No longer simply covering a surface, or maintaining the arrangement characteristic of normal glandular

tissue, they break through their natural confines (*e.g.*, basement membrane) and penetrate in irregular fashion the surrounding tissues.

From the manner in which the carcinomata push out bud-like processes, or 'roots,' in all directions, the term 'cancer' (=crab) has been given to them.

This activity of the epithelial cells is accompanied by a proliferation of the connective tissue cells of the part, this apparently occurring in response to some chemical irritation associated with the epithelial cells.

There is thus developed a tumour composed of a fibrous stroma containing in its meshes loose epithelial cells. The

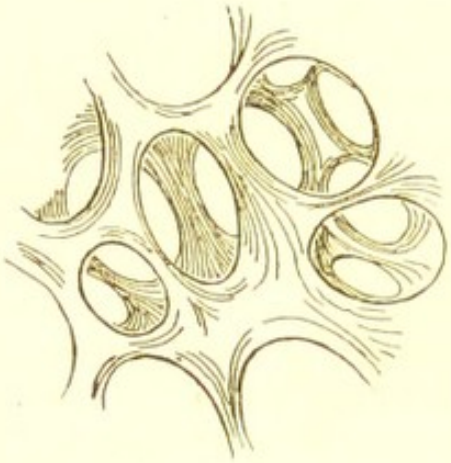

FIG. 9.—STROMA OF CARCINOMA (CORNIL ET RANVIER).

spaces in which these are contained are in reality dilated lymphatic spaces, and they thus communicate with the neighbouring lymphatics; sometimes they constitute large intercommunicating alveoli filled with lymph ('cancer juice'), the epithelial cells either lying free within them (scirrhus and encephaloid), or lining the alveolar walls (columnar epithelioma).

The fact that the spaces in which the carcinoma cells (epithelia) are contained are simply dilated lymphatics explains how it is—

(*a*) That the extension of the tumour peripherally takes place not only along the intercellular lymphatic clefts, but also along the issuing lymphatic vessels; thus the tumour thrusts out in all directions processes or roots extending far beyond its visible confines.

(*b*) That the carcinoma cells are apt to be carried away from the tumour and to lodge in the lymphatic glands draining the tumour area, there to set up secondary growths which reproduce the features of the primary growth. The looser the cells, the greater will be the tendency for them to be carried away. Thus secondary growths occur more readily in the case of scirrhus and encephaloid than in the case of epithelioma.

The epithelial cells of carcinoma tend to resemble those of the part from which they grow. Thus, a carcinoma of the lip contains squamous cells; of the intestines, columnar cells. If, however, they are subjected to much pressure from abundant stroma-formation, they are liable to deviate from the original type.

Carcinoma is liable to undergo degenerative changes, the most common being 'colloidal' and 'fatty' of the epithelial cells, and myxomatous degeneration of the stroma. When the tumour involves a surface, such degeneration leads to ulceration. In this case (and often in cases in which the breaking down of the tumour is unattended with ulceration) a mixed infection of the tumour takes place, leading to toxæmia. Cancerous cachexia (anæmia, emaciation, and pigmentation of the skin) results chiefly from this, and partly from long-continued discharge, and partly also from the appropriation by the tumour of nutriment which should go to nourish the normal tissues. Whether the malignant tumour before it degenerates, or becomes the seat of mixed infection, gives off poisons capable of producing cancerous cachexia is doubtful.

The transference of cancer from one human being to another has never been satisfactorily observed, neither has a tumour from man ever been successfully inoculated into a lower animal. Experimentally considered, the case stands thus:

'The transplantation of a spontaneous tumour into the same animal, either subcutaneously or intraperitoneally, is almost invariably successful, although transplantation into other animals of the same species may fail in extreme cases in as many as 500 attempts. This difference obtains whether the other animals are normal (young or old), or are exactly comparable by being naturally cancerous and of the same stock and same age. Thus, of 55 reinoculations of animals with their own tumours, 54 were positive; whereas of 77 inoculations of spontaneous

tumours in other spontaneously affected mice, only 5 were positive. If transplantation of a spontaneous tumour be practised under the most favourable conditions, as described in published papers, the percentage of success rarely reaches 30 per cent., and on the average is only 12 per cent. From such observations we must conclude that animals naturally the subject of cancer do not suffer from it because they present a soil uniformly favourable to the disease. On the contrary, the circumstances associated with the appearance and the growth of cancer are in each case peculiar to the individual attacked, and need not be similar to that obtaining in any other individual. Further, these experiments would go a long way to prove that the cancer cell, although highly dangerous to the individual in which it arises, is relatively innocuous to other individuals. This conclusion is not vitiated by the ease with which other tumours, after artificial adaptation to propagation, can be made to grow in all mice inoculated. In their case also it has been demonstrated that the risk of natural transference is non-existent.

'It is now possible, under given experimental conditions, to prevent a secondary transplantation—*i.e.*, artificial metastasis—taking place for certain tumour strains. This result has been obtained by inserting between the primary and secondary transplantations an inoculation of a very rapidly growing tumour showing only transitory growth, as the following sample experiment shows: Of twelve mice, already bearing progressively growing tumours and treated in the manner described, the secondary inoculation was successful in three only, and then the tumours were very much smaller than in the control consisting of thirteen mice, of which ten developed new progressively growing tumours on secondary inoculation. A similar result can be obtained by the implantation of tumours growing much more slowly and liable to spontaneous absorption, as well as by an inoculation of normal mouse tissue. By similar methods the growth of the primary transplanted tumour may be greatly hindered, can be brought to a standstill, and the animal cured, in circumstances under which the disease would certainly have progressed, and where the possibility of the occurrence of spontaneous cure can almost certainly be excluded. Thus the control of transplanted cancer has been brought within the region of probability' (Report of the Executive Committee, Cancer Research Fund, July 20, 1910).

In the same Report we learn that in the case of animals the factor of heredity in connection with cancer is almost a negligible quantity.

A **Squamous Epithelioma** grows from parts covered by stratified squamous epithelium (skin, mouth, tongue, pharynx, œsophagus, larynx, vulva, vagina, lower part of

cervix uteri, bladder, penis, and anus). There is a down-growing of the epithelium, branching processes of epithelial cells, derived from the deeper layers of the epidermis, boring their way through the tissues, like the roots of a tree through the soil. This invagination of epithelium may be regarded as an abortive attempt at tubular gland formation. Unlike what happens in columnar carcinoma, the tubes remain solid.

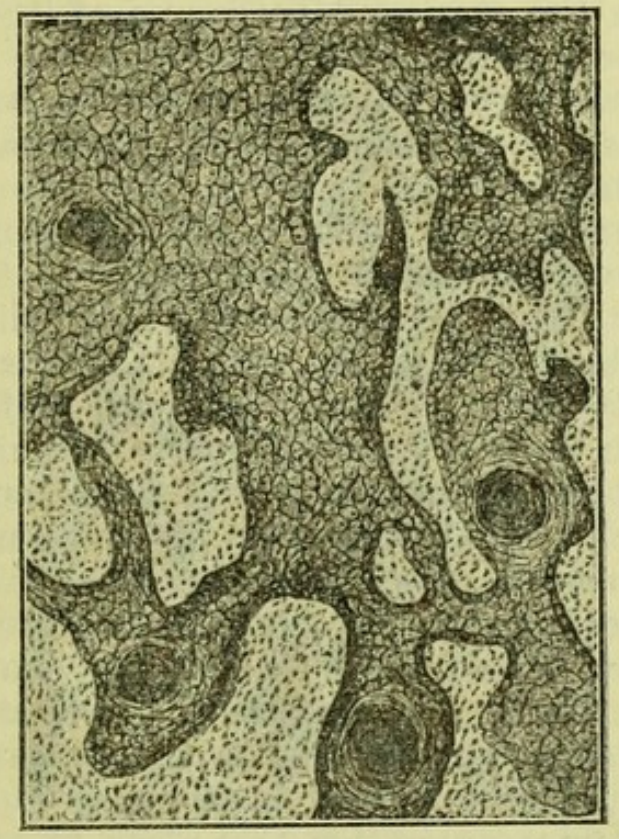

FIG. 10.—SQUAMOUS EPITHELIOMA, SHOWING CELL-NESTS.

It is these down-growing processes of epithelial cells which, when viewed on transverse section under the microscope, constitute the so-called 'cell-nests'—onion-like masses of cells having the following structure: In the centre are flattened dried-up cells; around these are layers of crescent-shaped cells, and on the outside columnar-shaped cells resembling those of the rete Malpighii. (This order represents the tendency of the cells to undergo their normal epidermic evolution.) In course of time the whole cell nest becomes a mass of flattened cells arranged con-

centrically around the cornified centre. The fibrous stroma is scanty, rich in cells, and often shows leucocyte infiltration.

The tumour first appears as a small warty growth, which soon breaks down in the centre, forming an ulcer with very hard, raised, everted edge and indurated floor.

The group of lymphatic glands draining the area of the growth are infected more rapidly when the primary growth is situated in soft vascular parts (*e.g.*, tongue) than when occurring in the skin and in course of time they may become cystic, involve the skin, and ulcerate. *No secondary growths occur beyond these lymphatic glands as a rule*, probably because the intercepted epithelia, being comparatively large, cannot escape beyond the infected glands. Squamous epitheliomata frequently originate from chronic ulcers, sinuses, and scars.

A **Rodent Ulcer** is a species of epithelioma growing from the sebaceous glands, sweat glands, or hair follicles, and generally occurring above a line drawn from the angle of the mouth to the lobe of the ear. Common situations are the root of the nose and the neighbourhood of the eyelids. The growth begins as a small nodule in the skin, which soon breaks down into an ulcer with a smooth, depressed floor, and a hard, raised, everted, sharply-cut, sinuous edge. The disease extends very slowly, and may go on for many years, gradually destroying the tissues both superficially and in depth. In this way it may eat its way through bone and even penetrate the brain itself.

It is not uncommon for the ulcer to make abortive attempts at healing, but the scar tissue which forms soon breaks down.

Structurally a rodent ulcer resembles an ordinary epithelioma, but the individual cells are smaller, and in most specimens cell-nests are absent, or, when present, ill-developed.

The epithelial cells of the growth are prevented from escaping into the lymphatic glands; these are not affected, and dissemination into distant organs never occurs, the malignant cells being fixed.

Spheroidal-celled (or **Alveolar**) **Carcinoma** is typically represented in the ordinary cancer of the breast. A fibrous tissue stroma encloses well-defined intercommunicating

alveoli—whence the name 'alveolar'—packed with epithelial cells, spheroidal or polygonal in shape, all of which float freely in a fluid—the so-called cancer juice (see Fig. 9). In course of time the growth invades the pectoral fascia and skin, eventually ulcerating on the surface.

There are two chief varieties, depending upon the relative proportions of cells and stroma. If the stroma is dense and abundant, while the cells are not plentiful, the tumour is hard and is called *scirrhus;* if the stroma is sparse and the cells are abundant, the tumour is soft and from its resemblance to brain tissue is termed *encephaloid.*

The area of infiltration of the tumour is usually much greater than the clinical signs would suggest.

In the case of scirrhus the primary growth may be small in comparison with the secondary growths, which grow with great rapidity, and are always of the encephaloid variety.

In mammary carcinoma the lymphatic glands of the *pectoral* group are soon infected, and later on the *axillary*, the *infraclavicular*, the *supraclavicular*, and the *subscapular;* the disease may also be transmitted to the *sternal* glands and so to the *mediastinal* glands and other parts. As the lymphatics anastomose across the middle line of the chest, the glands in the opposite axilla are sometimes involved.

Duct Cancer (or **Villous Cancer**) grows from the epithelium of the ducts of the breast (generally not far from the nipple). It is composed of a fibrous stroma enclosing alveoli. The alveoli are lined with (*i.e.*, not, as in scirrhus and encephaloid, entirely filled by) columnar epithelium, and into their interior vascular papillary processes are seen to project. Owing to the rupture of the bloodvessels in these processes, the alveoli often contain much extravasated blood, which may escape by the nipple.

Duct cancers are of slow growth; they are not so liable as other forms of carcinoma to affect the glands or to recur after removal.

Paget's Disease of the Nipple resembles chronic eczema in its naked-eyed appearance, but is in reality a slowly growing *carcinoma*, commencing around the orifices of the lactiferous ducts, and gradually spreading along the skin and into the deeper structures.

A **Columnar-celled Carcinoma** is a tumour growing from the positions where normally columnar cells are met with—*e.g.*, the mucous membrane of the stomach, intestines, liver, pancreas, and uterus (body and upper part of the cervix).

It consists of alveoli lying in a fibrous stroma; but, instead of the alveoli being packed with cells, as in ordinary epiblastic carcinoma, they are, as in duct cancer, *lined* with columnar epithelium, enclosing a central space; a columnar-celled carcinoma in this respect resembles an

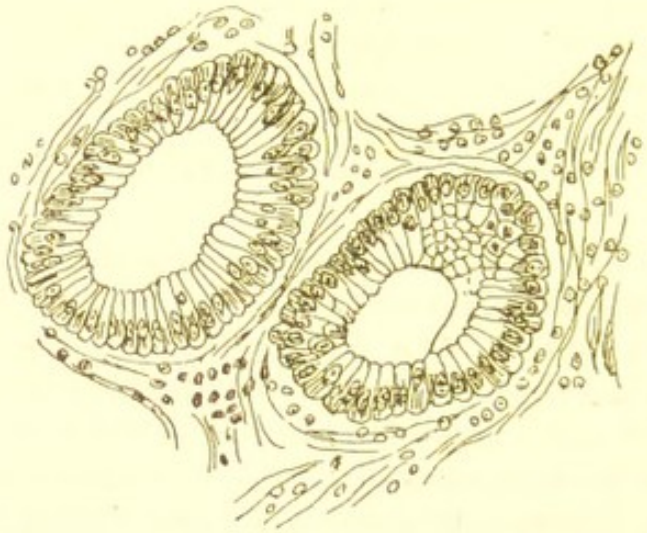

FIG. 11.—COLUMNAR-CELLED CARCINOMA.

adenoma: hence the old name of *adenoid cancer* applied to it.

It differs, however, from an adenoma in that it lacks definition, is devoid of a capsule, infiltrates the neighbouring tissues, ulcerates with extreme readiness, tends to recur after removal, and gives rise to secondary growths.

In the alimentary tract it generally grows as a ring around the canal, constituting the so-called 'ring carcinoma.'

Columnar-celled carcinomata show a marked tendency to *colloid* degeneration, especially when occurring in the stomach.

Colloid Cancer is simply one of the preceding forms (generally the encephaloid or columnar-celled), the epithelial cells of which have undergone colloid degeneration.

This is common in the cancers of the stomach, intestines, and ovary.

Melanotic Cancer.—In this very rare form of carcinoma the pigment (melanin) is usually confined to the stroma. It generally grows from a pigmented mole which has been subjected to prolonged irritation. It is intensely malignant by virtue of its rapid dissemination through the lymphatics. The primary growth may remain small and unnoticed, the first indication of its existence being a rapid enlargement of the related lymphatic glands. The secondary growths are likewise pigmented. The usual sites are the sole of the foot and the matrix of the nail of the great-toe. (This tumour was formerly mistaken for melanotic sarcoma.)

The Incidence of Cancer in Relation to Age, Sex, and Situation.

On analyzing 6,732 cases of cancer occurring at the Middlesex Hospital between the years 1746 and 1904, Dr. Lazarus-Barlow found that the mean age of incidence in males was 55·2 years, and in females 49·9 years. In males 80 per cent. of all cases of cancer occurred in the alimentary tract, while in females 80 per cent. were found in the generative organs and breasts. Cases of cancer of the alimentary tract were seven times as frequent in males as in females (see Fourth Report from the Cancer Research Laboratories, Middlesex Hospital).

After the age of thirty-five, one in eight females, and one in twelve males, die from carcinoma.

DISEASES OF THE VEINS.

Varix (Varicose Vein).

Varix consists of a permanent yielding of the venous wall, both laterally and longitudinally, in consequence of which the vein becomes dilated and elongated—it may even become as large as the wrist and three times its normal length. In consequence of the elongation the vessel is tortuous. The walls undergo a compensatory thickening, and when cut crosswise the vessel gapes like a divided artery. It is probable that the essential cause of

varix, when it occurs idiopathically, is a defect in the venous muscular coat, *which normally, by its tonic contraction, resists the distending action of the blood-pressure* more effectually than any mere passive tissue can. This is, indeed, the essential function of the venous muscular coat, which is thickest where venous blood-pressure is greatest—*i.e.*, the lower limbs (Campbell). Either we must suppose that there is a congenital defect of the muscular coat in those predisposed to varicosis, or that its muscle fibres remain unduly relaxed, and thus fail to brace up the venous walls in normal fashion. The most notable change observed in the wall of the varicose vein is the replacement of its normal elements by fibrous tissue. Here and there the wall is thinned and dilated into pouches, over which the skin may become adherent. The valves undergo cicatricial contraction, ultimately shrinking considerably, and even disappearing. In course of time there may be no competent valves between the affected vein and the right heart, and this explains *the 'impulse' on coughing* which may sometimes be felt in a varicose vein.

Complications:

Pigmentation of overlying skin.
Thrombosis.
Phlebitis.
Adhesion to skin.
Ulceration (varicose ulcer).
Perforation.
Eczema.
Œdema of the ankle.

A dilated pouch adherent to the skin may give way by ulceration, or even by bursting without previous ulceration. Dangerous bleeding then ensues, which may prove fatal in a few minutes. This bleeding takes place in a different way from ordinary hæmorrhage; for, the dilated vein being rigid and not collapsing, and the valves being incompetent, the blood comes *largely—indeed, chiefly—from the cardiac side* of the perforated vessel: it is a reflux.

Occasionally calcareous plates are met with in the thickened walls of a varicose vein, and in rare cases *phleboliths* may form in the interior.

The veins commonly affected by varix are the internal and external saphenous, the pampiniform plexus of the spermatic cord, and the hæmorrhoidal veins.

Sometimes a varicose vein is not much lengthened—*e.g.*, the internal saphenous vein may stand out as a more or less straight dilated tube from the ankle to the groin. In such cases we must assume that the longitudinal muscle fibres are functionating normally.

Phlebitis is inflammation of the venous wall, and is always associated with thrombosis.

There are two classical forms of phlebitis—(*a*) the infective or suppurative, and (*b*) the simple or non-suppurative.

(*a*) In *Infective Phlebitis* the venous wall becomes inoculated with pyogenic organisms, and a clot soon forms inside the vessel. The cause may be a septic wound, extension of inflammation from some neighbouring septic focus, such as acute infective osteomyelitis, middle-ear disease, or carbuncle, especially when it occurs on the face.

The venous wall, the surrounding tissues, and the thrombus inside the vein, are crowded with septic micro-organisms. The clot breaks down, and septic emboli may be discharged into the blood-stream, and so lead to pyæmia, unless a ligature be placed on the proximal side of the clot.

In favourable cases infection of the blood-stream is prevented by the portion of the clot at the proximal end remaining firm instead of disintegrating.

(*b*) *Simple Phlebitis*, like the infective variety, is always associated with thrombosis. The thrombosis may cause the phlebitis, or the phlebitis may cause the thrombosis, but the two pathological conditions always coexist.

The causes are thrombosis (see Thrombosis), injury, extension of surrounding inflammation, and certain blood states—the 'gouty phlebitis' of Paget, for example. Varicose veins, especially when superficial, are more liable to inflammation than healthy ones.

The coats of an inflamed vein are infiltrated with small round cells, the endothelium is swollen and may become detached, and, in the case of superficial veins, œdema of the surrounding tissue is observed.

In all inflamed areas the walls of the small veins are involved in the inflammatory process.

Terminations of phlebitis:

Resolution of the clot and obliteration of the vessel.
Organization.
Tunnelling—*i.e.*, the axial part of the thrombus is absorbed, and the peripheral part organizes.
Embolism.
Suppuration.
The formation of phleboliths.

DISEASES OF THE ARTERIES.

Acute inflammation of an artery may be the result of trauma, infection from septic wounds, or by septic emboli. Excluding these, the classical forms of arteritis are—

Acute endarteritis—Acute aortitis.
Arteritis in inflamed area.
Chronic endarteritis:
- Atheroma, or endarteritis deformans
  - Secondary calcification.
  - Atheromatous abscess.
  - Atheromatous ulcer.
- Primary calcification.
- Endarteritis syphilitica.
- Endarteritis obliterans.
- Endarteritis tuberculosa.

Acute Endarteritis.—The best example of this rare disease is *acute aortitis*, which is usually the result of infection from the aortic valves in malignant endocarditis. In other cases it results from blood infection. Its usual situation is at the beginning of the aorta and round the origin of its branches.

The process commences as a small round-celled infiltration of the inner coat, producing sharply-defined, raised, gelatinous patches, circular or ovoid in outline, and soft and elastic in consistence. The infiltration may extend into the middle and outer coats, in which case the new elements may organize into fibrous tissue. The endothelium, as a rule, remains intact.

The disease may lead to aneurism, or pass into endarteritis deformans.

Arteritis in Inflamed Area.—When an area of tissue is inflamed, the tissues constituting the walls of the arteries and veins within the inflamed area share in the inflammatory process. The inflammatory changes are even more marked in the venous walls than in the arterial. The arterial and venous walls, notably the adventitia and

intima, become infiltrated with cells, and in this way the lumen of the affected vessels become narrowed, and even obliterated, thrombosis being thereby induced. At a later stage the new cell formation may organize into connective tissue, causing a permanent hardening of the vessels.

Atheroma and Endarteritis Deformans are described by different authors in different ways. In the following account the two terms are used as meaning the same thing.

Atheroma is common in men over forty with high blood-pressure, especially in connection with granular kidney. Except as a senile change, it is, indeed, rarely met with in subjects displaying low blood-pressure. The connection between atheroma and high blood-pressure is further shown by the fact that the former is seldom, if ever, met with in the pulmonary circuit, except when, from disease of the left heart, the blood-pressure in that circuit has been chronically augmented. Again, atheroma never occurs in the systemic veins except as the result of a long-sustained augmentation of venous pressure.

Many consider that microbic infection plays an important part in the etiology of atheroma. It was once thought to be due to the obliteration of the vasa-vasorum, but Cowan has shown this view to be incorrect.

The disease occurs in those arteries which are exposed to the greatest strain, as in the arch of the aorta and at the points at which large branches are given off, or where a trunk bifurcates, the most frequent sites being—

The aortic arch.
Round the orifice of its large branches.
The coronary arteries.
Round the orifice of the cœliac axis.
At the bifurcation into the iliacs.
The cerebral arteries.
The renal arteries and their branches.

As it affects the Aorta and Large Vessels.—Small round cells, in the form of scattered foci, infiltrate the *intima*, replacing the normal elements of the part. In course of time these foci coalesce to form pale yellowish, semi-gelatinous patches, slightly elevated above the surface. The further progress may be in one of two

directions: the patches may (*a*) calcify, or they may (*b*) soften and break down.

(*a*) In the former case fatty degeneration of the cells takes place; the contents afterwards dry up, and lime-salts and cholesterin are deposited in the shrivelled mass, which is thus ultimately converted into a hard, calcareous plate. This is known as *secondary* or *laminar calcification*, so called to distinguish it from the primary annular calcification found in the middle coat of such arteries as the radials and tibials. At this stage the interior of the vessel is seen to be studded with hard, milky, circumscribed, non-vascular patches. On careful inspection, the endothelium is generally found to be intact, however advanced the process.

(*b*) On the other hand, the contents of the patches, instead of drying up, may liquefy and form an *atheromatous abscess*, which, upon the endothelium giving way, may become converted into an *atheromatous ulcer*. Should this latter form, a small coagulum will form over the roughened part.

Besides the involvement of the intima in atheroma, cellular infiltration into the middle coat may take place, while the outer coat may be the seat of a varying amount of compensatory fibroid thickening.

So long as the intima alone is affected, the vessel wall is not likely to yield before the pressure of the blood; but directly the muscle fibres, which by their active contraction prevent the vessel from undergoing progressive yielding before that pressure, are implicated, the damaged part of the vessel is liable to yield slowly, and thus lead to the formation of an aneurism.

As it affects the Smaller Vessels (*Coronary, Cerebral, Renal, etc.*).—The process here is essentially the same as in the case of the large vessels. The patches, however, are often in the form of nodes, sometimes suggesting in appearance a 'signet-ring,' which may project so far into the lumen as partially to occlude it.

It is to be specially noted that in atheroma *there is no formation of new bloodvessels*, hence the tendency to degeneration. Atheroma thus stands in marked contrast to syphilitic endarteritis.

Primary Calcification affects the medium-sized arteries

—*e.g.*, those distributed below the elbow and knee. The process begins in *the middle coat*, the muscle fibres of which become infiltrated with lime-salts, and as these fibres run circularly round the vessel, the deposit takes the form of a succession of rings, causing the artery to assume the appearance of ipecacuanha. Ultimately the artery may be converted into a rigid tube. In the case of the tibial arteries, the intima may actually become detached, and as a result of this thrombosis and gangrene may occur (see Senile Gangrene). *Symmetry is a marked feature of the disease.*

Endarteritis Syphilitica.—Disease of arteries is one of the most important manifestations of syphilis. The pathological change is identical in principle with the syphilitic affections of other mesoblastic structures. In one class of case there occurs a diffuse gummatous infiltration of the intima, which extends both around the vessel and along its course for some distance. This in process of time develops into concentric laminæ of fibrous tissue. In another class of case small greyish-yellow patches may be seen on the interior of the vessel; these are gummata. In both instances the intima becomes greatly thickened, and the lumen correspondingly narrowed.

Owing to the existence of new capillaries, fatty or calcareous degeneration does not occur.

The disease is most common in the *arteries at the base of the brain and in the arteries of gummata* (see Gummata). In consequence of the narrowing of their channels, thrombotic occlusion is liable to occur; this is the most frequent cause of hemiplegia (especially in men) under forty years of age, and also explains the tendency of gummata to slough.

'The discovery of the pathology and symptomatology of syphilitic arteritis has been one of the most important advances in modern medicine' (Mott). The disease may arise in the early stage of the secondary period, or at any subsequent time.

Endarteritis Obliterans is probably an advanced stage of endarteritis syphilitica. There is great subendothelial proliferation, the change involving also the middle and external coats. New capillaries are formed, and the final result is the formation of fibrous tissue, which narrows

the lumen and may ultimately occlude it. In some cases occlusion is brought about by thrombosis.

Endarteritis Tuberculosa generally involves the perivascular lymphatic sheaths, but tubercles may also develop *in* the arterial walls themselves. Under these circumstances the intima becomes greatly thickened, and the lumen reduced in size and even obliterated.

Arterio-Sclerosis.

Apart from the diseases just dealt with, there is a condition of the arteries associated with advancing years which is commonly known as *arterio-sclerosis*.

Old age is a relative term, and, medically considered, is to a large extent determined by the condition of the arteries—*i.e.*, whether they are soft and elastic, or hard and rigid.

After a certain period of life the arteries, in common with the other tissues, tend to harden. This results from a general fibrosis, which impairs the normal elasticity of the vessel walls, and makes them rigid. This increase in the fibrous elements of the vessel wall is especially observed in the intima, the thickness of which tends to increase from puberty until the end of life. The test of a healthy artery is that if such a vessel as the radial or temporal be pressed by the finger it melts away into, and can be scarcely differentiated from, the surrounding tissues, whereas a thickened vessel can be distinctly felt under the examining finger. There is no precise age at which the senile change comes on. Sometimes the arterio-fibrosis sets in early. A man of thirty, for instance, may have the arteries natural to a man at sixty, and *vice versa*. Hence the aphorism, 'A man is as old as his arteries.' Thomas Parr is said to have had arteries which at the time of death showed nothing abnormal.

In connection with this subject of arterio-sclerosis (or fibrosis) the student is referred to pp. 148, 149, dealing with the arterial changes observed in granular kidney.

Early arterial degeneration runs in families. Renal disease, errors of diet, alcohol, toxæmias, heredity, and other influences, all play their part in the production of premature arterio-sclerosis.

Cerebral Hæmorrhage (Apoplexy).

Much the most frequent cause of cerebral hæmorrhage is rupture of miliary aneurisms occurring in subjects of chronic Bright's disease. Other causes are infective embolism from ulcerative endocarditis, causing localized arterial softening, syphilitic arteritis, intracranial aneurism (macroscopic), and cerebral tumours.

Ordinary cerebral hæmorrhage is four times more frequent in the male than in the female sex.

Aneurism.

An aneurism (*aneurisma*, a dilatation) is a cavity communicating with an artery and containing blood, either fluid or coagulated. The walls of the cavity are formed either of the expanded portion of the vessel wall, or of the tissue around.

It is during the middle period of life, between the ages of thirty and fifty, that aneurism is most frequently met with.

In children aneurism is probably always due to embolic arteritis.

'Dissecting' aneurism is more common in women than in men; aneurism of the carotid is equally common in the two sexes; otherwise aneurism is thirteen times more common in men than in women.

Classification.

Spontaneous	Fusiform.
	Sacculated.
	Dissecting.
Traumatic	Circumscribed.
	Diffuse.
Arterio-venous	Aneurismal varix.
	Varicose aneurism.

A **Spontaneous Aneurism** is one that develops in consequence of pre-existing disease of an artery.

A *Fusiform Aneurism* is a dilatation involving the entire circumference of the artery, the result of *extensive disease of its walls*. The usual seat is the arch of the aorta. As a rule, the vessel is involved for a considerable portion of its length. In addition to the dilatation there is *elongation*, which may be considerable. Thus, the arch of the aorta may be increased in length by some inches. From the main dilatation small 'saccular' aneurisms may spring.

On examining the structure of a fusiform aneurism, it will be found that the internal coat shows widespread atheromatous changes: it is stiff and rough, calcareous plates are frequently scattered over the internal surface, and in places where the endothelium is injured shreds

of fibrin are adherent. The middle coat is atrophied in proportion to the degree of dilatation. The outer coat is compensatorily thickened and strengthened by the formation of new fibrous tissue. It is owing to this thickening that the course of an uncomplicated fusiform aneurism is usually chronic—either remaining stationary or increasing very slowly, and thus continuing for many years without causing death.

A *Sacculated Aneurism* is one in which the dilatation involves only a part of the circumference of the artery, the result of a *localized* disease of its walls. When the aneurism is of very small size, the three arterial coats are spread out over it; when somewhat larger, the internal coat is wanting; when it attains a still larger size, the middle coat is also absent, and the sac of the aneurism is then constituted by the external coat strengthened by a thickening of the surrounding connective tissues. Usually the interior of a sacculated aneurism contains fibrin arranged in concentric, overlapping layers, no single layer reaching over the whole sac. The older layers on the outside are of a pale buff colour, those towards the interior are darker.

Organization of the clot is rare, because of the forcible stream of blood through the aneurismal sac. *No organization can take place in the aneurism unless the artery from which it springs is occluded.* Occlusion may occur either by extension of the clot from the sac into the artery, by a detached piece of clot plugging the artery, or as the result of surgical compression or ligature.

Complete arrest of the circulation leads to the formation of an ordinary soft blood-clot (*clot en masse*); this is very rare, however, and is only possible when the mouth of the aneurism, or the main trunk of the artery immediately beyond it, becomes plugged by a detached piece of clot.

Causes of Death from Aneurism.—The tendency of aneurisms is to *rupture*, either into the pericardium, pleura, trachea, œsophagus, peritoneum, or externally very rarely. *Embolism* (*e.g.*, of the cerebral arteries) may occur in consequence of the detachment of a portion of the clot into the blood-stream. Death may also result from *pressure* on vital parts.

Ætiology of Spontaneous Aneurism.—It can be definitely stated that the essential cause of 'fusiform' aneurism is a preceding widespread atheromatous change in the artery (especially such as destroys the middle coat), for evidence of this is always present in the walls of the dilated portion. In a 'sacculated' aneurism, however, the case is different, for owing to the small area from which the aneurism springs, and the fact that but little of the arterial coats remains in the sac wall, the exact nature of the local disease which starts the process is difficult to determine. Atheroma and the degenerations resulting from syphilis and alcohol, coupled with the strain of heavy muscular exertion, are the chief factors in the causation. In short, those who worship at the shrines of Venus, Vulcan, and Bacchus are the most liable to spontaneous aneurisms.

An important function of the muscular coat of arteries and veins, practically the sole function in the large arteries and veins, is by its *active contraction* to prevent dilatation. *Passive* tissue must perforce yield to long-continued pressure. We should therefore expect the essential cause of aneurism to be a weakening of the muscular coat.

A *Dissecting Aneurism* is one in which there is a longitudinal rupture of the internal coat, the blood being forced between the layers of the middle coat. It is generally the result of the bursting of an atheromatous abscess. The blood may escape by an aperture in the outer coat and become diffused externally, or it may open again into the lumen of the artery through another atheromatous spot. It is most common in the aorta, and occurs more frequently in women than in men.

A **Traumatic Aneurism** is a cavity containing blood, either fluid or coagulated, communicating with an artery, and produced by an injury dividing all the coats of the vessel.

If the blood escapes slowly, compression of the tissues around leads to the formation of an adventitious sac, and the result is a *circumscribed traumatic aneurism.* On the other hand, if the blood escapes quickly and in abundance, it finds its way along the connective-tissue planes, travelling in the direction of least resistance, and the distending force being too great to allow of the formation of a sac, a *diffuse traumatic aneurism* results.

Miliary Aneurisms are about the size of a small pin's head, and are met with in the cerebral arteries, more especially those coming off from the circle of Willis—

i.e., the *central* as distinguished from the *cortical* arteries. It is from rupture of such a miliary aneurism that 'spontaneous' cerebral hæmorrhage is practically always due. When this occurs in a child, it is generally from an aneurism which has developed secondarily to a septic embolism.

The pathology of miliary aneurisms is still somewhat doubtful. Charcot taught that they do not occur secondarily to atheroma; that, whereas this condition starts in the intima and spreads outwards, the arterial change which leads up to miliary aneurism begins in the external coat of the artery and spreads inwards. Certain it is that atheroma of the cerebral vessels may be extensive and miliary aneurisms conspicuous by their absence from them, and *vice versa*. One clinical fact stands out prominently in connection with miliary aneurisms: they never occur in association with low blood-pressure. Hence the low blood-pressure individual does not die from cerebral hæmorrhage.

Miliary aneurisms, if they do not rupture, tend in course of time to become occluded, from thrombosis of their contained blood and subsequent shrinkage.

An **Arterio-Venous Aneurism** is the result of a communication between an artery and a vein lying in juxtaposition. It is generally of traumatic origin—*e.g.*, when the brachial artery and the median-basilic vein at the bend of the elbow are wounded simultaneously.

If the two vessels are in close contact and become adherent, the blood passes directly from the high blood-pressure artery into the low blood-pressure vein, and the latter becomes dilated into a pulsating, fusiform, or globular pouch, with thickened walls, the dilatation extending also into the venous tributaries, which become varicose and tortuous. This is known as *aneurismal varix*.

Instead of the blood passing directly from the artery into the vein, it may well out between the two tubes, and become enclosed in an adventitious sac communicating with both. This condition is known as *varicose aneurism*.

SHOCK

The terms 'shock,' 'syncope,' and 'fainting' all mean practically the same thing. The pathology of shock concerns essentially the cardio-vascular system. There occur:

Paralysis of the vaso-motor centres, particularly of those controlling the splanchnic area—this allowing the blood to accumulate in the portal system of veins ('bleeding into one's own veins').

Enfeebled Cardiac Action.—A less quantity of blood enters the heart, which in consequence loses the stimulus of the normal endocardial pressure.

The output of the left heart being less than normal, the arteries are underfilled, and this explains the thready pulse (often irregular and intermitting), the cold and clammy skin, with fall in the surface temperature, and the arterial anæmia of the brain, which renders the patient partially unconscious.

It will be seen that, according to the view here enunciated, shock (syncope, or fainting) is not due to a primary paralysis of the heart, but to a widespread arteriolar dilatation, the heart being secondarily affected.

It should be remembered that life itself depends upon the maintenance of an adequate degree of arteriolar tonus.

The exciting causes are—

Mental, such as an emotion;
Physical, such as severe trauma.

The degree of shock varies with—

The nervous susceptibility of the patient; and
The severity of the injury.

COLLAPSE.

The pathology of collapse consists essentially in the *loss of fluid* from the blood.

Collapse accompanies such diseases as are attended by constant vomiting or diarrhœa, examples being the diarrhœa of young children, Asiatic cholera, and the

profuse and prolonged vomiting of strangulated hernia and acute peritonitis. Owing to the abstraction of such large quantities of fluid, the blood becomes inspissated and resembles tar, and the muscles, liver, spleen, and kidneys become tough and leathery.

Collapse may also result from severe hæmorrhage.

DISEASES OF THE PERICARDIUM.

By pericarditis is meant an inflammation beginning in the *serous* pericardium. It can generally be traced to the action of some bacterial toxins—*e.g.*, those generated by the *Diplococcus rheumaticus* (much the most frequent cause), and the toxins developed in connection with pyæmia, septicæmia, the specific fevers (scarlatina), pneumonia, tubercle. It also occurs in association with Bright's disease (when it is always fatal), and as a result of the extension of disease from surrounding parts (*e.g.*, burns on the thorax, mammary cancer).

In the following description, rheumatic pericarditis is taken as the type. The inflammation starts at the base of the heart, travels downwards, and involves more or less the entire pericardial sac.

The smooth, glistening surface becomes dull and sticky from swelling of the lining endothelium and the exudation of inflammatory lymph. Coagulation of the lymph now takes place, and by the rubbing together of the opposed surfaces the interior of the pericardium comes to present a 'shaggy' appearance. The pericarditis may be 'dry,' or fluid may collect in the pericardial sac. The effusion rarely exceeds 2 to 3 ounces in quantity. (The increased area of cardiac dulness found in rheumatic fever is *mainly due to cardiac dilatation*, and not to pericardial effusion.) After a time, new bloodvessels penetrate the fibrinous exudate, connective tissue forms, thus uniting the visceral and parietal layers of the pericardium.

The adhesions thus formed may be slight or extensive, *but in some degree they always form in pericarditis*, so that the sac becomes partially or wholly obliterated. From repeated attacks the pericardium may become greatly thickened, even to the extent of ½ inch. Sometimes there

is an associated *mediastinitis*, and when this happens the pericardium may become adherent to the sternum, ribs, lungs, and diaphragm. The phrenic nerves in some of these cases lie embedded in the newly-formed fibrous tissue.

The heart, especially the left ventricle, is always dilated in rheumatic pericarditis. This has been ascribed to direct extension of the inflammation to the myocardium ; others, with more probability, attribute it to the paralyzing action of the rheumatic toxin on the cardiac muscle, for dilatation is absent in other forms of pericarditis (*e.g.*, tubercular, suppurative), while it is always present in rheumatic fever, even when there is no pericarditis.

Should the patient be allowed to get up too soon there is great risk of the dilatation becoming permanent. Such dilatation of necessity leads to hypertrophy, as, the cubic capacity of the ventricle being increased, more work is required of it. This dilatation with secondary hypertrophy mainly accounts for the enormous hearts sometimes found in adherent pericardium, the adherent pericardium, *per se*, playing but a subordinate part. If, on the other hand, the patient has been allowed adequate rest in bed, so that the dilatation and the hypertrophy which it entails have had time to subside, and if the pericardium is not greatly thickened, there may be no permanent cardiac enlargement.

To sum up, then, the cardiac enlargement sometimes found after an attack of rheumatic fever may be due to—

(*a*) A dilatation remaining permanent.
(*b*) A much thickened pericardium.
(*c*) A combination of both.

It is to be remembered that endocarditis and myocarditis often coexist with pericarditis.

Purulent pericarditis is rare. It occasionally occurs in connection with empyema, septicæmia, pyæmia, pneumonia, and scarlatina, or it may result from extension of malignant growths. It is extremely rare in the rheumatic pericarditis.

Blood is sometimes found in the pericardium as the result of pericarditis, septicæmia, pyæmia, scurvy, and purpura, as also from rupture of an aneurism.

Tuberculosis of the Pericardium.—This is very rare, even when tubercles abound elsewhere. When found, it generally

occurs in association with tubercular pleurisy, and tubercular mediastinal glands.

The effusion may be serous, purulent, or hæmorrhagic.

In old-standing cases, calcified plates may form in the walls of the pericardium.

DISEASES OF THE HEART.

Weight of heart:

Adult male, 10½ ounces.
Adult female, 9½ ounces.

'The thickness of the walls of the various cardiac chambers is as follows:

'That of the *left ventricle* varies from ¼ inch at the apex to ½ or ¾ inch at the auriculo-ventricular furrow.

'That of the *right ventricle* varies from ⅛ inch at the apex to ¼ inch at the auriculo-ventricular furrow.

'That of the *left auricle* measures about ⅛ inch.

'That of the *right auricle* measures about $\frac{1}{12}$ inch' (Box).

The heaviest heart on record weighed 55 ounces; the lightest was under 2 ounces.

Simple Endocarditis.

This disease is usually confined to the endocardium of the valves, and may be either:

(*a*) *Acute*, or
(*b*) *Chronic.*

(*a*) **Acute Simple Endocarditis.**—Except when occurring during fœtal life, it is almost always confined to the valves of the *left heart.*

It is a disease mainly of early life, and probably 90 per cent. of the cases are due to rheumatic fever. Any other infection, however—*e.g.*, scarlatina—may cause it.

The liability to endocarditis in rheumatic fever may be expressed thus: It begins at the age of two years, is crescendo from two to ten years, and diminuendo from ten to forty years, after which period the liability practically disappears.

Order of incidence:

Mitral valve alone.
Mitral valve and aortic valve.
Aortic valve alone.

It begins on, and is generally confined to, that surface of the valve which faces the blood-current—*i.e.*, the auricular surface of the mitral and the ventricular surface of the aortic valve.

The endothelial cells swell up and become detached. Rows of minute glistening beads form a short distance from the free edge of the valve. These beads are technically known as 'vegetations,' and are composed of blood-platelets (*vide* p. 19), and entangled in a meshwork of fibrin.

Results of Acute Endocarditis :

Resolution.
Organization, contraction, and hence regurgitation.
Fusion of valve-edges, and hence stenosis.
Aneurism of valve.
Rupture of a valve aneurism.
Detachment of vegetations, and so embolism.
Contraction of chordæ tendinæ.

(*b*) **Chronic Endocarditis.**—This condition must be distinguished from the damaged condition of the valve left by acute endocarditis. It is a chronic, progressive process from the start, leading to fibrosis and often atheromatous changes. It is rarely found under the age of thirty.

The *Aortic Valves* are those *par excellence* affected. The causation may be expressed thus : *Syphilis*, *alcoholism*, *physical strain*, acting either singly or in conjunction, and high arterial blood-pressure (an almost constant factor).

The valve-segments, more particularly at their free margins, become thickened, opaque, puckered, and distorted from the formation and contraction of scar tissue. This causes the valve to 'leak.' Calcareous material may be deposited in the valves, especially near their attached margins.

Disease of Individual Valves.

Mitral Valve.—Disease of this valve is generally the result of rheumatic fever, the usual sequel being retraction of the valve-edge, with consequent escape of the blood backwards—*i.e.*, mitral regurgitation.

Mitral Regurgitation.—The left auricle is dilated and somewhat hypertrophied; the left ventricle is dilated and hypertrophied. As the disease progresses the lungs have a difficulty

in emptying their blood into the left heart, and there result: venous congestion of the lungs (with 'red' or 'brown' induration from fibrosis and pigmentation); dilatation and slight hypertrophy of the right ventricle; tricuspid regurgitation; dilatation of the right auricle; impeded portal circulation, causing venous congestion of the liver ('nutmeg' liver), which may pulsate; congestion of the mucous membrane of the gastro-intestinal tract, of the peritoneum (causing ascites), and of the spleen (the splenic enlargement, unlike what we find in primary portal obstruction—*e.g.*, hepatic cirrhosis—is moderate); congestion of the kidneys (and thus albuminuria and diminished flow of urine); œdema, beginning in the lower limbs and mounting upwards, and involving the trunk, upper limbs, head, and neck. As the œdema increases so the urine decreases. Should the valve guarding the junction of the internal jugular and subclavian veins 'leak,' there is pulsation of the veins in the neck.

In the dilated right heart a thrombus may form, which, if it breaks up, causes embolism of the lungs (pulmonary apoplexy).

Mitral Stenosis.—When coming under observation the patient is generally a young woman. As in mitral regurgitation, the chief cause is rheumatic fever, although a history of this disease can but seldom be obtained, probably because the form which causes mitral obstruction is less obtrusive (subacute [?]) than that which causes mitral regurgitation (the joint symptoms in the rheumatic fever of children are often vague, and may be entirely absent). The valve segments are glued together at their margins, producing either the 'button-hole' orifice or the 'funnel-shaped' orifice of Corrigan. The apex of the funnel looks in the direction of the blood-current—*i.e.*, into the ventricle.

(The writer has shown that both these forms of orifice are hydrodynamicall constructed with a view to oppose a minimum of resistance to the blood-flow.)

The obstruction at the mitral orifice causes hypertrophy (which in early cases may be considerable) of the left auricle; later dilatation, often extreme, occurs. A clot is liable to form in the left auricular appendix, a portion of which becoming detached may give rise to embolism. This is the commonest cause of embolism of the middle cerebral artery. The lungs are congested, as in mitral regurgitation, but the tendency to hæmoptysis is much greater. (Sometimes such cases of hæmoptysis are mistaken for *phthisis.*) The pulmonary arteries are often atheromatous. The right ventricle is dilated and hypertrophied. In course of time tricuspid regurgitation, with all its secondary consequences, ensues.

Many contradictory statements have been made regarding the condition of the left ventricle in mitral obstruction: in pure cases it is of normal size. The fingers are more apt to become clubbed than in mitral regurgitation. Patients rarely reach the age of forty.

The Aortic Valve.—Disease of this valve alone, though sometimes a sequel of rheumatic fever, is more often of the nature of a chronic endocarditis, in which case there is usually atheroma of the aorta at the same time. Isolated aortic valve disease (*i.e.*, without affection of the mitral valve) is rare as the result of rheumatic fever; if present in a young woman, it is nearly always of syphilitic origin.

Aortic regurgitation is the usual sequel, aortic stenosis being rare.

In aortic regurgitation the blood is squirted backwards during diastole by the recoil of the stretched aortic walls, the initial result being dilatation of the left ventricle, to be immediately followed by compensatory hypertrophy. This dilatation and hypertrophy tend to be progressive, causing the heart to assume enormous dimensions (*cor bovinum*). As the result of increased intraventricular pressure, the mitral orifice may 'leak' (either from stretching of the orifice or curling up of the valve curtains), when all the sequelæ of mitral regurgitation ensue. The endocardium lining the septum of the left ventricle at the point of impact of the regurgitant blood often shows patches of thickening.

At a later stage *fibroid* degeneration of the heart muscle is liable to occur, in accordance with the general law that a muscle is capable only of a certain amount of hypertrophy, and when this limit is reached, muscular atrophy and fibroid degeneration follow.

As in all diseases of the heart, the measure of the patient's danger is the condition of the cardiac muscle.

Aortic Stenosis.—This is rare, and when found results from either an acute endocarditis or from atheromatous thickening. The left ventricle is hypertrophied, dilatation being superadded in course of time. (N.B.—What is clinically often called aortic stenosis is generally nothing more than a murmur, caused either by 'roughening' of the valves, or atheroma of the aorta.)

Tricuspid Valve.—'Leakage' at the right auriculo-ventricular orifice is generally the result of the 'back-wash' of mitral disease (regurgitation or stenosis), or of chronic lung disease—*e.g.*, emphysema and bronchiectasis. Simple endocarditis of the valve rarely occurs except during fœtal life. If the tricuspid becomes diseased during extra-uterine life, it is generally from malignant endocarditis.

The Pulmonary Valve.—The common lesion of this valve is *stenosis*, which is practically always congenital, the result either of a fœtal endocarditis or of a developmental defect. If occurring *early* in fœtal life, it is liable to be associated with a deficiency of the upper part of the interventricular septum (*pars indefensa*), the two ventricles then communicating. Endocarditis of the pulmonary valve occurring during extra-uterine life is almost always of the malignant variety.

Malignant Endocarditis.

This form of endocarditis is due to the action of virulent organisms, amongst the most important of which are pneumococcus, *Streptococcus pyogenes aureus*, gonococcus, and the influenza bacillus. There appears to be a malignant form of rheumatic endocarditis, but whether this is due to the organism of rheumatic fever or to a mixed infection is uncertain.

Special Characters.—The disease attacks by preference damaged valves (*i.e.*, those affected by an old endocarditis); the vegetations are large, numerous, and highly friable; the valves may become aneurismal, and they may rupture. *Sometimes the valves of the right heart are involved.* The infection may spread to the walls of the heart, the aorta, and the chordæ tendinæ. Owing to the friability of the vegetations, they frequently give rise to embolism, more especially of the spleen, kidneys, and brain.

The heart tissue generally shows a polymorphonuclear infiltration, with cloudy swelling and granular degeneration of the muscle fibres.

Diseases of the Heart Musculature.

Atrophy.—This occurs in old age and in certain wasting diseases, such as phthisis and diabetes. The muscle fibres shrink, granules of golden-brown pigment are deposited in their interior (chiefly around the nuclei), the heart assumes a brownish colour—hence the name *brown atrophy of the heart* applied to this condition.

The nature of the pigment in brown atrophy of the heart is a disputed point. It appears to be either *melanin* or a pigmented fat (*lipochrome*).

Hypertrophy.—This develops in response to the necessity for increased work on the part of the cardiac pump, *and is only possible when the nutrition of the heart is good.*

Hypertrophy without dilatation is rare. Hypertrophy with diminution of the cardiac chambers is a post-mortem effect.

Hypertrophy of the Heart as a Whole. — This is typically seen in certain cases of adherent pericardium.

Causes of hypertrophy of the *left ventricle*:
- Aortic regurgitation.
- Aortic stenosis.
- Mitral regurgitation.
- Increased peripheral resistance—*e.g.*, in chronic renal disease.
- Excessive muscular exercise.
- Exophthalmic goitre.
- Aneurism.

Causes of hypertrophy of the *right ventricle*:
- Mitral disease.
- Emphysema, Bronchiectasis } And other chronic lung diseases.
- Diseases of the pulmonary valves.
- Pressure on pulmonary artery (aneurism, etc.).

Pure hypertrophy of the right ventricle never lasts long. This is probably due to the comparatively low reserve power of its musculature.

Hypertrophy of the ventricles is said to be *concentric* when it occurs without dilatation, and, except in pure aortic stenosis, is but rarely seen. When the hypertrophy is associated with dilatation, it is said to be *eccentric*, and such is the usual form.

Hypertrophy of the auricles is always associated with dilatation, the left auricle being most affected in mitral stenosis, and the right auricle in emphysema and disease of the mitral valve.

Dilatation, or increase in the cubic capacity of one or more of the heart chambers, may either precede, or succeed, hypertrophy, the two conditions then coexisting.

If a heart of good reserve power is exposed to conditions imposing on it increased work, the initial result is hypertrophy, followed by dilatation if the cause be long-continued. For example, the greatly hypertrophied left ventricle of chronic Bright's disease tends in course of time to dilate. (Most cases of hypertrophy are, however, from the very beginning accompanied by some degree of dilatation.) If, on the other hand, a heart of low reserve power be exposed to conditions of increased strain, the tendency is rather to dilatation pure and simple.

Acute cardiac dilatation occasionally occurs. It is probable that the acute pain of an attack of angina

pectoris is due to the stretching of the heart walls arising from an acute dilatation of the left ventricle. Acute dilatation of the left ventricle is the rule in rheumatic fever, and particularly so in the case of children, its cause being a toxic poisoning of the cardiac musculature.

Mechanism of Cardiac Dilatation.—The essential factor in the mechanism of cardiac dilatation is excessive distension of a cardiac chamber during diastole. (It is manifest that a cardiac chamber cannot yield during its systole.) The causes of such excessive diastolic distension are—

(*a*) Regurgitation of blood into a chamber, which thus receives blood from two directions.

(*b*) Inadequate systole, leading to an excess of residual blood in the inadequately systolizing chamber. This is the great cause of cardiac dilatation in failing heart—*e.g.*, in the later stages of granular kidney. Degeneration of the cardiac walls leads to dilatation in this way, and also by rendering them liable to yield.

(*c*) An excessive supply of blood from the normal direction—*e.g.*, in sprinting, the blood may be driven into the right heart by the rhythmical contractions of the muscles more rapidly than it can be delivered into the lungs. The dilatation of the left ventricle in mitral regurgitation results from the extra supply of blood this chamber receives from the dilated left auricle.

Diseases of the Coronary Arteries.

Although the arteries of the heart anastomose to a slight extent, they may, for all practical purposes, be regarded as 'terminal.'

Atheroma.—The coronary arteries are especially liable to this disease. Their channels are narrowed, and the heart substance, receiving an insufficient supply of blood, tends to undergo fatty and fibroid degeneration.

Thrombosis.—This is a not infrequent complication of atheroma. Its results are the same as those of embolism (see below).

Embolism.—If a large vessel is blocked, the usual result is sudden death; if a small vessel is blocked—short of causing death—an *infarct* results. Should the patient live sufficiently long, the infarct is converted into fibrous

tissue. This, subsequently yielding to the intracardial pressure, causes an *aneurism of the heart*, the common site of which is in the region of the apex of the left ventricle.

Syphilitic Endarteritis.—This causes great narrowing of the channels of the affected vessels, and, like atheroma, is liable to be complicated by thrombosis. According to Osler, it is the commonest lesion to be found post mortem in angina pectoris.

Fibroid Heart.

This form of cardiac degeneration occurs in connection with disease of the coronary arteries, as a terminal event in the hypertrophy and dilatation of valvular disease, general arterial fibrosis, as well as in syphilis.

Fibrous tissue forms between the muscle fibres, in part replacing them. The change is usually confined to the left ventricle, and occurs more particularly in the neighbourhood of its apex. It is one of the causes of sudden death.

Fatty Degeneration of the Heart.

In this disease fat globules, often arranged in rows, appear in the muscle fibres. The change is most marked in the left ventricle. In typical cases the heart looks 'mottled,' like the thrush's breast.

Three main factors (which may act singly or in conjunction) are probably concerned in its causation—the action of some toxin, disease of the coronary arteries, and the want of an adequate supply of oxygen. It is to be remembered that the heart requires more oxygen than any other tissue in the body.

Chronic alcoholism is perhaps the commonest of all causes. Alcohol is not only a protoplasmic poison, but it interferes with the oxygenation of the tissues. Other causes are: prolonged and severe anæmias (it is always present in pernicious anæmia), phthisis, and phosphorus-poisoning.

As an acute condition, it is found in diphtheria.

Heart-Block (Stokes-Adams Disease).

By heart-block is meant that condition in which the contraction wave from auricle to ventricle is 'blocked.'

The 'block' may be slight, the ventricular beat lagging behind the auricular, or so marked that the auricles and ventricles beat quite independently of each other.

The experimental work of Gaskell, supplemented by that of Erlanger, has shown that the contraction wave from auricles to ventricles is transmitted, not through nervous influence, but by a specialized bundle of fibres (His's bundle), of the shape of an inverted Y, which, beginning in the interauricular septum, passes down to the interventricular septum, at the bottom of which it bifurcates, each arm then spreading out over the whole interior of its respective ventricle. The bundle of His is supplied by a separate branch of the right coronary artery.

The cause of the disturbance of the cardiac rhythm is a lesion of the bundle of His, blocking its continuity, the commonest lesion being *syphilitic*, either gummatous or fibroid degeneration of the fibres, or disease of the artery supplying them.

The clinical picture of Stokes-Adams disease is: persistent slow pulse (bradycardia), with a tendency to syncope, vertigo, and epileptiform attacks—all of which latter symptoms result from irregularity and insufficiency of the cerebral circulation, the ventricle at times missing fire, as it were—the conduction of the contraction wave from auricle to ventricle being 'blocked.' Inasmuch as digitalis and strophanthus impair the conductivity of the bundle of His, the administration of these drugs is strongly contra-indicated in Stokes-Adams disease.

DISEASES OF THE LUNGS.

The lungs are developed as outgrowths of the œsophagus. The epithelium lining the air cells, bronchi, and trachea is derived from the hypoblast, and the rest of the lung tissue from the mesoblast.

Collapse of the Lung.

Atelectasis is the condition of the lungs in the stillborn. Such lungs are completely airless and sink in water.

The causes of collapse of the lungs are:

1. Pressure from without the lungs { air, serum, pus, blood, aneurism, tumours.

2. Obstruction from within the lungs, caused by blockage of the bronchial tubes.

The chief cause of such obstruction is 'capillary bronchitis,' in which the small tubes become plugged with viscid mucus. The imprisoned air is absorbed by the blood, and the alveolar walls, falling together, ultimately lie in contact.

Collapsed lung is reduced in size, of a dark red colour, and non-crepitant ; it sinks in water.

Pulmonary Emphysema.

Pulmonary emphysema may be defined as a rarefaction of the pulmonary tissue, either in the form of simple distension of the air vesicles, or as an actual running together of them by absorption, or rupture of the intervening septa. The elasticity of the pulmonary tissue is defective.

There are two main varieties—the *spurious* and the *true*.

In *spurious* emphysema (insufflation, acute emphysema) the lungs may remain unduly expanded for some days, but there is no rupture of the air vesicles. It occurs chiefly in children, as the result of capillary bronchitis and catarrhal pneumonia. In these diseases excessive stretching of the uncollapsed air vesicles occurs as the combined result of widespread vesicular collapse, and of the thoracic expansion (from preponderating action of the inspiratory muscles) resulting from dyspnœa. As a result the vesicles are so greatly stretched as temporarily to lose their power of recoil.

Of *true* emphysema there are two kinds : the *interlobular*, in which, under the influence of a violent expiratory effort, actual rupture of the vesicles takes place, the air escaping into the interlobular spaces, and

thus gain access to the mediastinum and thence to the subcutaneous tissue of the neck and chest; and the *vesicular*, in which adjacent vesicles run into one another.

Vesicular Emphysema.—This is the variety which is generally meant when pulmonary emphysema is referred to. It may occur in a localized or generalized form. In the former it is met with in the neighbourhood of pleuritic adhesions, or in parts of the lungs which have been rendered airless—*e.g.*, by tubercle or collapse—when it is generally known as *compensatory* emphysema. In these localized forms the essential cause is undue traction on the vesicular walls, in consequence of which their nutrition fails and the septa between adjacent vesicles give way.

In generalized vesicular emphysema a degeneration of the vesicles takes place throughout the entire lungs; their bloodvessels and epithelial lining atrophy; they lose their elasticity; and the septa between adjacent vesicles give way. At the same time the vesicular walls lose their wavy outline, presenting under the microscope a stretched appearance.

This variety of emphysema is essentially due to *primary atrophic degeneration.* Such degeneration takes place in everyone with advancing years, quite independently of cough, but in some it is met with in early adult life or even before this. Its occurrence is favoured by certain diseases, such as gout and granular kidney.

The second, but much less important, factor in the production of this form of emphysema is *long-continued overstretching of the vesicular walls.* Such overstretching may result from (*a*) excessive pressure from within, as happens when a powerful expiration is made while egress to the air is impeded, as by a completely or partially closed glottis (muscular effort, coughing), or in blowing wind instruments. Or it may result from (*b*) excessive traction from without. We have seen that the latter is the chief factor in determining localized emphysema. Such traction may also be a minor factor in causing generalized emphysema; in all forms of breathlessness other than those due to obstruction in the respiratory passages (as by the diphtheritic membrane or by throttling), the mean size of the chest is increased by

the preponderating action of the inspiratory muscles (the expiratory muscles remaining in partial or complete abeyance). This is because the inspiratory position of the chest is the one most favourable to the pulmonary circulation and the aeration of the blood (Campbell). Hence whatever promotes breathlessness predisposes to emphysema, whether it be physiological breathlessness, such as results from athletic pursuits, or pathological breathlessness, such as occurs in asthma and heart disease.

In generalized emphysema the lungs may be unduly expanded (hypertrophous, or 'large-lunged,' emphysema), or (much less frequently) not more than their average size (atrophous, or 'small-lunged,' emphysema). In the latter case it is probable that the disease has not occurred until the thoracic cage has undergone senile fixation. When it occurs before this, the mean size of the chest (owing to the favouring influence of the inspiratory position on pulmonary circulation) undergoes steady increase from overaction of the inspiratory muscles (Campbell). As a result, these latter shorten (just as the overacting muscles do in talipes), and so fix the chest in the inspiratory position. Moreover, the bones and joints of the thorax tend to become 'set' in this new position. In this way the chest, in the latter stages of the disease, may be fixed in a position of super-extraordinary inspiration—*i.e.*, the patient is unable, by the most powerful expiratory effort, to reduce his thorax to normal dimensions.

It will be observed that the enlargement of the chest in 'hypertrophous' emphysema is compensatory. A reduction of the chest to the normal size in this condition would soon cause death.

It will generally be found that the chest expands as middle life is reached, especially in stout people. Men are apt to pride themselves then on possessing a 40-inch chest, ignorant of the fact that such a measurement generally indicates degeneration. The progressive enlargement takes place in obedience to the principle already enunciated, and is in large measure due to loss of pulmonary elasticity. In order to maintain physiological conditions it is necessary that the pulmonary tissue shall be kept in a certain degree of tautness (for otherwise not

only will 'pulmonary suction' fall below the normal, but the slack, wrinkled vesicles will unduly encroach upon the air spaces), and as the pulmonary fibres lengthen they need to be tightened up—tuned up to the normal pitch, so to speak—by an increase in the mean size of the chest.

Though generalized vesicular emphysema involves the entire lungs, the emphysema is usually most marked at the parts least supported during occasions of heightened intra-pulmonary pressure—*i.e.*, the apices, anterior margins, lower and posterior margins (which may present an appearance which has been likened to the fur on a lady's mantle). It must not be forgotten that under ordinary conditions the lungs, far from being supported by the structure circumjacent to them, actually exercise suction upon them.

Owing to the loss of their elasticity, the lungs in generalized emphysema collapse but little when the thorax is opened, or when they are removed from the body. The anterior borders are found to have lost their sharp edges and to be rounded, showing emphysematous bullæ ('frog's lung'). They may also overlap in front, and by covering the heart obliterate the area of superficial cardiac dulness.

The pulmonary tissue is pale and bloodless, pits more easily than healthy lung tissue, and feels like eider-down. The air can be squeezed from one part to another with greater facility than normally.

As the emphysema progresses, the obstruction to the pulmonary circulation resulting from obliteration of the smaller vessels causes the branches of the pulmonary artery to dilate, and its main trunk often to become atheromatous. *Eventually the right heart becomes dilated,* and general venous congestion supervenes (enlargement of liver, œdema of lower extremities, albuminuria, etc.).

Bronchiectasis.

In this condition there is permanent distension of the bronchi, which in consequence may become—

Cylindrical,
Fusiform, or
Saccular.

The ætiology of bronchiectasis is much the same as that of emphysema—viz., increased stretching of the bronchial walls, either from augmented internal pressure (an unimportant factor) or increased traction from without (the essential factor). In bronchiectasis, however, another factor comes into operation—*i.e.*, weakening of the bronchial walls from degeneration of their muscular fibres, which (as in the case of all the muscular tubes of the body), by their active contraction, normally tend to prevent overstretching.

Bronchiectasis is the usual accompaniment of all fibroid diseases of the lungs, and is *typically met with in fibroid phthisis*. In this disease the contraction of the fibrous tissue, attached to the adherent pleura on the one hand, and to the bronchi on the other, has been held to be an important factor in causing the dilatation. Though such contraction plays its part, the chief traction comes from the powerful action of the inspiratory muscles, which, in accordance with the principle already mentioned, are in dyspnœa continually striving to increase the mean size of the chest. It is evident that were the normal amount of vesicular structure present without any fibrosis, such inspiratory action would simply lead to emphysema, because the delicate vesicular walls would necessarily yield before the stouter bronchi. When, however, the lungs are seamed with comparatively non-yielding fibrous tissue, the effect of the constant inspiratory efforts will be to expand the bronchi as well as the vesicles.

In bronchiectasis the muscular coat of the dilated bronchi is in large measure replaced by a fibrous tissue, and the mucous membrane tends to lose its sensibility. As a result, the secretion of the tubes is apt to accumulate and to undergo putrefaction, not being expelled until it reaches a level at which the mucous membrane is sufficiently sensitive to excite the act of coughing.

Bronchiectasis may give rise to abscess in the brain.

Pneumonia.

There are two classical forms of acute pneumonia, which have different exciting causes, run different clinical

courses, and present different morbid appearances. These are—

Lobar pneumonia, and
Broncho-pneumonia.

Lobar Pneumonia (Croupous).—*The pneumococcus of Fraenkel is the essential cause*, though occasionally the pneumo-bacillus of Friedlander, streptococci, and staphylococci are also present. The pneumococci are constantly found in large numbers in the mouth, pharynx, and nasal cavities of man in health, and it is only when vitality is depressed (*e.g.*, by chronic alcoholism) that they can set up inflammation of the lungs. They are most numerous in the advancing area of disease.

The lesion usually begins at the root of one lung, extending thence to the base, and in typical cases involves the whole of the lobe in a uniform manner.

The constitutional symptoms are the result of absorption of the *pneumo-toxin* into the system.

Lobar pneumonia is *always a pleuro-pneumonia*, and passes through the following stages:

The Stage of Congestion.—The affected area of lung is swollen, of a deep red colour from vascular engorgement, and it is less crepitant and less elastic to the feel than normally. It floats in water. The capillaries in the alveolar walls are distended, the lining epithelial cells swell up, and exudation of inflammatory lymph begins. Signs of pleurisy are evident.

The Stage of Red Hepatization.—The inflamed portion of lung, usually a whole lobe, is now solid, like a piece of liver; the inflammatory lymph has completely filled the alveoli and undergone coagulation, the clot being composed of a fibrinous network, entangling in its meshes leucocytes, chromocytes, and shed epithelial cells. In consequence of this the inflamed lung is distended, and its pleural surface may be indented by the ribs. (This is probably a post-mortem phenomenon, as during life the inspiratory muscles enlarge the chest on the affected side, and thus protect the inflamed lung from pressure.) The affected tissue does not crepitate, is very friable, and sinks in water. On section it looks like red granite, being dry and granular. The pleura is sticky and covered with lymph.

The Stage of Resolution may now occur, in which case the coagulum disintegrates, to be in part absorbed by the lymphatics and in part removed by expectoration; or, instead of resolution taking place at this period of the disease, the inflammation may pass on to

The Stage of Grey Hepatization.—The lung remains solid, is still more friable than in the second stage, and sinks in water. On section it looks like grey granite, and may yield a puriform fluid. The fibrinous network has now dissolved, the chromocytes have disappeared, and the alveoli are packed with leucocytes.

If at this stage a section of the lung is made from apex to base, the organ will be seen to be mapped out into zones. At the bottom is the zone of grey hepatization, while above this are three others—first, a zone of red hepatization, above that a zone of congestion, and above that, again, a zone of œdema.

Abscess.—In some cases of pneumonia the alveolar walls disintegrate, leaving a cavity filled with dead leucocytes. This is a very rare phenomenon.

Gangrene.—In persons whose tissues are very much weakened by, *e.g.*, alcoholism, the intensity of the inflammation may be such as to cause gangrene.

Complications.—The pneumococci entering the circulation may set up pericarditis, malignant endocarditis, meningitis, synovitis, or otitis media. The pleurisy may pass on to empyema (which is generally on the left side).

The absence of leucocytosis in pneumonia usually means a fatal termination. The expectoration of prune-juice-coloured sputum is also a bad sign, as it indicates much pulmonary œdema. At the time of the crisis the opsonic index undergoes a marked rise.

Chronic Pneumonia.—In rare cases the process becomes chronic; the alveolar walls become infiltrated with small round cells, which organize into fibrous tissue. There results an induration of the affected portion of lung, with which is apt, in course of time, to be associated emphysema and bronchiectasis.

Broncho-Pneumonia (Catarrhal, Lobular Pneumonia).—This disease is *always preceded by a preliminary capillary bronchitis*, of which it is the direct outcome.

It is microbic (pneumococci, streptococci, and staphylococci) in origin, and an example of point-to-point infection. Thus, it occurs in children as the result of measles, whooping-cough, and scarlatina, and in adults after influenza and operations on the mouth and windpipe ('aspiration' and 'deglutition' broncho-pneumonia). The inspired air rendered septic by passing over the infected mucous membrane of the mouth, nose, or pharynx, sets up a capillary bronchitis; subsequently, patches of pneumonia develop around the affected bronchioles, in consequence of—

Direct extension of the inflammation; or

Inoculation with septic material from the bronchioles; or

Collapse of the alveoli from plugging of their bronchioles with mucus and subsequent absorption of the imprisoned air.

Possibly all these factors co-operate.

A section of such a lung in an early stage of the disease shows small, dark red, ill-defined patches, ranging in size from a pin's head to a pea, *and surrounding inflamed bronchioles*, separated by healthy intervening lung tissue. At a later stage neighbouring patches may coalesce and a large and continuous area of consolidation result. Pleurisy is less common than in lobar pneumonia, and is found only in those cases in which the patches lie adjacent to the surface.

The bronchioles are inflamed, and filled with mucus and shed epithelium. The air vesicles are packed with cells—chiefly swollen epithelial cells—also leucocytes in variable numbers, and a few chromocytes. In some of the alveoli a fibrin network may be present.

Tubercular Broncho-Pneumonia is *par excellence* the lesion of phthisis.

Phthisis, or Pulmonary Tuberculosis.

The tubercle bacilli derived from dried-up sputum, or dust, invade the pulmonary tissue by two main paths:

Via the tonsils, the cervical glands, the mediastinal, and the bronchial glands, and thence to the peribronchial lymphatics.

Via the alimentary tube and thoracic duct.

The tubercle bacilli at length settle in the lymphatics of the lung (peribronchial, perialveolar, and perivascular), where, liberating their toxins, anatomical tubercles form, as explained on p. 72.

The cardinal initial lesion in all cases of phthisis is probably a tubercular broncho-pneumonia.

Although no two cases of phthisis are ever precisely identical, we may in a general way describe four chief types:

1. Chronic, or ordinary phthisis.
2. Acute phthisis.
3. Acute miliary tuberculosis.
4. Fibroid phthisis.

1. **Chronic Phthisis.**—This is the ordinary form of pulmonary tuberculosis. There are three definite stages:

(*a*) *Consolidation.*—Tubercles form in the peribronchial, perialveolar, and perivascular lymphatics of the apex, setting up a broncho-pneumonia, and causing a portion of the lung to become solid.

(*b*) *Excavation.*—The pressure exerted by the perivascular tubercles, plus the action of the bacterial toxins, cause thrombosis of the bloodvessels in the consolidated area: hence result necrosis, caseation, and cavity formation. A cavity thus produced is called a *vomica*. A cavity may also be caused by the yielding of the softened tubercular bronchial walls (bronchiectasis).

(*c*) *Fibrosis.*—*Pari passu* with excavation new fibrous tissue forms on the outside of the diseased area, the adjacent pleura thickens, and by becoming adherent to its opposite layer seals up the intrapleural space.

Recently-formed cavities have irregular walls of softened necrotic tissue, while older ones are lined with a smooth pus-yielding membrane, often darkly pigmented. They contain pus, degenerated endothelial cells, lung débris, and caseous matter.

If a branch of the pulmonary artery passes along the wall of a cavity or across its lumen, it is generally obliterated by thrombosis. Sometimes, however, it remains patent, and in this case an aneurism may form in the vessel, and by rupturing give rise to severe, even fatal, hæmorrhage.

Should the disease become arrested, more fibrous tissue

is formed, which, contracting, partially or completely seals up the cavity, converting it into a pigmented fibro-cicatricial mass enclosing calcareous matter.

If, on the other hand, the disease progresses, fresh areas of lung tissue are infected in succession, the processes of consolidation, excavation, and fibrosis are repeated again and again, and sooner or later the other lung becomes similarly affected.

2. **Acute Phthisis (Galloping Consumption).**—This is a form of pulmonary tuberculosis that runs a rapid course, the patient dying within a few months.

The tubercular broncho-pneumonia is intense from the start, and numerous small cavities soon form, the interior of which consist of softened, necrotic, and caseous material. There is little or no tendency to the formation of an organized wall. Successive areas of pulmonary tissue are rapidly affected. If a cavity lies close to the surface it may ulcerate into the intrapleural space and cause pneumothorax and pyopneumothorax, no time having been allowed for pleural adhesion to take place.

3. **Acute Miliary Tuberculosis.**—In this disease an eruption of innumerable tubercles occurs throughout the substance of both lungs. It is probably never primary, *but always a final stage of a pre-existing tubercular lesion.* In this sense it is an auto-infection, the source of infection being, as a rule, caseating bronchial glands in the case of children, and in the case of adults an old tubercular deposit in the apex of one lung.

In acute miliary tuberculosis the bacilli are thought to be *carried by the blood-stream*, thus differing from other forms of tuberculosis, in which infection is conveyed by the lymphatics. The bacilli reach the blood either by the caseation of a gland into the walls of an adherent vein, or by the caseation of a tubercle which has formed on the outside of a bloodvessel. The bacilli cannot multiply while in the circulation, but only after coming to rest in the lymphatics of some organ.

Patches of broncho-pneumonia are scattered throughout the lungs, but death occurs before any marked destruction of tissue can take place. Owing to the rapidity of the process, no giant cells can usually be seen. Many other organs may be affected simultaneously with the

lungs. The disease is liable to be mistaken for enteric fever.

4. **Fibroid Phthisis** (**Cirrhosis of the Lung**) is a very chronic form of pulmonary tuberculosis, not usually developing until after the age of thirty, and lasting from ten to twenty years.

Fibrosis predominates over necrosis, the lung tissue being replaced to a greater or less extent by connective tissue, embedded in which are tubercles—often difficult to detect on account of the density of the new tissue: in most cases, indeed, the only evidence of their presence is the occurrence of giant cells. *This form of phthisis is always associated with marked bronchiectasis*, the bronchiectatic cavities being formed either of dilated bronchi or of broken-down lung tissue. In a fully developed case the lung is shrunken, hard, and fibrous. the pleura is thickened and adherent, and the organ feels like a cirrhotic liver. On section, the fibrous tissue is found to have penetrated both the alveolar walls and the interlobular septa, obliterating many of the air-vesicles. There is marked dilatation of the bronchi, which often open into spaces lined by a smooth, pus-secreting, membrane. The pleura outside these bronchiectatic cavities is flattened, for bands of fibrous tissue pass to it from the walls of the cavities, and by contracting cause depression of its surface (see Bronchiectasis).

In all cases of phthisis the lymphatic glands at the bifurcation of the trachea and those at the root of the lung are generally tuberculous.

The liver and heart are usually fatty in all forms of active phthisis.

The temperature in tuberculosis may remain afebrile throughout, and when it is raised, this is probably due to the presence of pyogenic organisms.

Pneumokoniosis (*konis*, dust).

This is a form of chronic interstitial pneumonia set up by the inhalation of irritating particles—coal-dust in miners (*anthracosis*), metal-dust in needle and knife grinders (*siderosis*), stone-dust in stonemasons (*silicosis*), which, passing into the lymphatics of the lungs, is deposited in various parts of these organs. Bronchial catarrh, patches of chronic catarrhal pneumonia, an

increase—sometimes considerable—of the fibrous tissue, pigmentation, pleural adhesions, and bronchiectasis, are the chief pathological features. These cases are very liable to be complicated by tubercle, and are then examples of fibroid phthisis.

Syphilis of the lung is very rare, and, when found, is usually in the form of gummata in the neighbourhood of the root.

In stillborn children, or those dying soon after birth, a diffuse fibrosis may be observed. In other cases a 'white pneumonia' may be present.

Glanders.—The *Bacillus mallei* may cause a broncho-pneumonia. The consolidated areas resemble septic infarcts.

Actinomycosis consists of grey nodules containing pus, in which are found the yellow grains of the streptothrix.

Tumours of the lung may be primary or secondary, and are practically always malignant.

Primary tumours are either carcinomata springing from the bronchial epithelium, or sarcomata growing from the lymphatic glands at the root, and travelling along the connective tissue planes in all directions.

Secondary growths (carcinomata and sarcomata) are multiple, and cause the lungs to assume a marbled appearance.

DISEASES OF THE NERVOUS SYSTEM.

A **neurone** is a cell provided with one or more processes and traversed by neuro-fibrils, which constitute the strands along which 'nerve currents' travel. Each neuro-fibril enters the neurone through one of its processes, traverses the cell-body, and leaves the cell by another process, or if there is but a single process (as in the case of the sensory neurones of sensory nerves), by the same process.

It will thus be seen that the essential elements of the neurone processes are neuro-fibrils. Two kinds of such processes are met with: (*a*) Shorter naked processes, or dendrites, which, after arborescing, terminate in free extremities within the grey matter of the brain and spinal cord; and (*b*) longer medulla-coated processes, or **axons**. These latter constitute the ordinary medullated nerve fibres met with in the white matter of the brain and spinal cord, and in the cerebro-spinal nerves. In the latter case, the medullated fibres have an additional sheath in the shape of the neurilemma, which, unlike the neurone proper (which is of epiblastic origin), is derived from the mesoblast, and is of the nature of connective tissue. The function of the medullary sheath is probably partly to protect, and partly to aid in the nutrition of, the neuro-fibrils constituting the central core, or axis cylinder, of the long axons. The neurilemma has similar functions, and, further, aids in the regeneration of nerve fibres after their division, whether by trauma or by disease (*e.g.* anterior poliomyelitis).

Neurones are contiguous, but not continuous; the neuro-fibrils do not pass from one neurone to another. Each neuro-fibril begins at the extremity of a neurone process, traverses the cell body, and ends at the extremity of a neurone process. One of these extremities is receptive (afferent) and adapted *to be stimulated;* the other is emissive (efferent) and adapted *to stimulate.*

The *afferent* extremity is provided with an end-organ, which is adapted to be stimulated by a specific form of stimulus, and thus

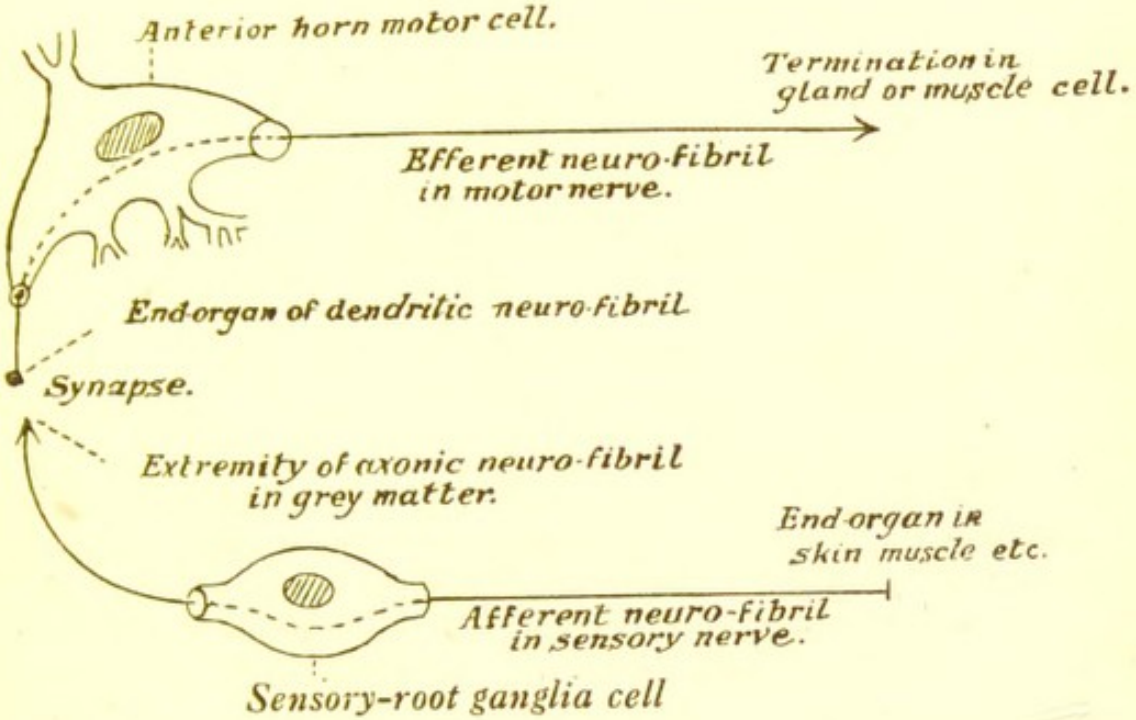

FIG. 12.

This diagram shows the course of the nerve impulses in a simple spinal reflex. For the sake of simplicity, the sensory root ganglion cell is represented as having two processes instead of one process, and the intermediary cell between the sensory root ganglion cell and the anterior horn motor cell is omitted.

to start a nerve current along the neuro-fibril. There are two chief classes of such afferent end-organs: those belonging to the neuro-fibrils of the sensory and special-sense nerve fibres, and those belonging to the dendritic neuro-fibrils situated in the grey matter of the brain and spinal cord.

The *efferent* extremities have similarly two modes of termination: The neuro-fibrils belonging to the axons of efferent nerves terminate in muscle fibres, or epithelial cells; those belonging to axons which end in the grey matter of the brain and spinal

cord have free extremities, which are placed in relation with the receptive end-organs of neighbouring dendritic neuro-fibrils.

Observe that on this view the function of the terminals of efferent neuro-fibrils (those, *i.e.*, which run in efferent axons) is to initiate a chemical process (for the most part of a disruptive nature) either in a muscle fibre, or gland cell, or in the receptive end-organ of a dendritic neuro-fibril.

The interval between the free extremity of an efferent axonic neuro-fibril and the end-organs of its related dendritic neuro-fibrils is spoken of as a synapse. It is here that the real mystery of nervous action resides; it is here that the complex processes of co-ordination (including inhibition) are effected, and it is probably in this region also that the physical correlatives of psychic processes take place.

Nerve currents, it will be observed, originate in the end-organs of afferent neuro-fibrils. The old view of the cell-body of the neurone being a kind of battery discharging nerve currents along its processes must be abandoned.

Changes in Neurones which follow upon Division of Cerebro-Spinal Nerve.

Peripheral Portion.—The changes here have for their object the emptying of the neurilemmal sheath, so as to make way for a new down-growing axis-cylinder from the central end. The contents are gradually absorbed by the action of substances (ferments, lysins) developed within the sheath; the neuro-fibrils of the axis-cylinder become separated, break up into granules, which are absorbed; the medullary sheath breaks up into blocks (=fragmentation), and these into smaller particles, which become absorbed; the nuclei of the neurilemma multiply. These changes constitute Wallerian degeneration.

Central Portion—(*a*) *Cell-Body.*—Within twenty-four hours of the section changes in the cytoplasm of the cell body are observed: it and its processes swell somewhat from the imbibition of fluid; the chromophyl particles (Nissl's granules) break up into fine dust and may disappear (chromatolysis). The nucleus moves towards the periphery of the cell-body.

Changes similar to these have been observed in the large cortical motor cells of Betz after transverse section of the cord.

(*b*) *The Axon.*—Just above the point of section, notable changes occur: the neuro-fibrils become separated,

presenting the appearance of a tress of hair; soon they take on active growth, throwing out branches having bulbous extremities. The growing fibrils are directed by chemotaxis through the new-formed granulation tissue, which unites the divided ends of the nerve towards the emptying sheaths of the distal portion. By the time the fibrils reach the neurilemmal sheaths, the latter have rid themselves of their contents, and are ready to receive them. The fibrils penetrate the sheaths, forming new axis-cylinders; thereafter new medullary sheaths are formed.

This remarkable power of repair possessed by the medullated fibres of the cerebro-spinal nerves is not observed in those of the brain and cord, a circumstance which has been attributed to the fact that the latter lack a neurilemmal sheath. These fibres are probably endowed with some power of repair, however, for when severed by disease, the neuro-fibrils of the central end show a tendency to sprout and form terminal bulbs, as in the case of divided nerves.

In *acute affections of the neurone body*—*e.g.*, acute anterior poliomyelitis—the changes are very similar to those just described, but more pronounced; there occur tumefaction, vacuolation, complete chromatolysis, distortion and dislocation of the nucleus, which may be extruded from the cell, in which case the entire neurone suffers permanent dissolution, and can never be replaced. Every neurone in the organism is laid down in the embryo, and is adapted to last a lifetime: it may thus outlast a century.

In *chronic affections of the neurone body* (*e.g.*, chronic anterior poliomyelitis) there is simple atrophy—diminution in the size of the cell and its processes, ending, it may be, in complete dissolution of the entire neurone. In such cases 'pigmentary atrophy' may occur, the body of the cell being reduced to a mass of pigment, bordered by a layer of protoplasm.

The neurone changes, both central and peripheral, which occur in *peripheral neuritis*, are similar to those which occur after section of a peripheral nerve; also the *secondary degeneration* of the cerebro-spinal medullated fibres, save that in this case there is no neurilemmal sheath to share in the changes.

The name *periaxial neuritis* has been given to a disease of the axon involving the medullary sheath in parts, but leaving the axons intact. It has been observed in the neuritis produced by lead and diphtheria, in the posterior spinal roots in cases of tabes, and in the sclerosed nodules of disseminated sclerosis.

Secondary Sclerosis.—When the proper nervous tissue of the central or peripheral nervous system degenerates and disappears, a secondary hyperplasia of the connective tissue takes place. In the case of the central nervous system this is spoken of as sclerosis. A familiar instance is the secondary lateral sclerosis of hemiplegia or paraplegia: the peripheral portions of the severed motor axons disintegrate, and the neuroglia grows into and fills up the spaces left by them. At first the new tissue consists of a large-meshed reticulum, but this in time is gradually converted into dense tissue.

Weigert's stain tints the myeline sheath deep blue; therefore, if a section of sclerosed cord is stained by this method, the sclerosed patches show up by their absence of coloration. Marchi's method of staining is based on the fact that osmic acid stains fat black.

Toxic Degenerations of the Nervous System.

A large number of diseases of the nervous system, both functional and organic, are due to the selective action of toxins on neurones. Thus, the convulsions of rickets are due to the action of a toxin (or toxins) probably generated in the alimentary tract, while all the organic 'system' lesions (*e.g.*, tabes dorsalis) are the direct result of specific toxins. Indeed, putting aside the primary senile degenerations of the neurone—those, namely, due to a genuine wearing-out process—neurone degeneration is very rarely spontaneous. It is practically always referable to an extrinsic cause, such as circulatory defect—*e.g.*, syphilitic endarteritis—or toxic action.

Selective Action.—The selective action of toxins on tissue elements is in no case so remarkably displayed as in that of the neurones. Not only does this selective action obtain as regards different groups of neurones, but also as regards different portions of the same neurone—

cell-body, axon, axonic terminal, dendrite, dendritic end-organ. Thus, progressive muscular atrophy is due to the action of a toxin upon the cell-body of a lower motor neurone; lead palsy, to the action of lead upon the axon of such a neurone; while urari causes paralysis by acting upon the motor end-plate.

The distribution of toxic nervous lesions is, however, not due merely to a selective action between neurone and toxin, but may result in large measure from a concentration of the poison in certain parts of the nervous system. Thus, in lead palsy the muscles chiefly affected are situated below the elbow, possibly because the poison is largely absorbed from this region. Again, the sub-arachnoid space appears to offer a favourable breeding-ground for the *Treponema pallidum*, and it is probable that the concentration of these organisms in the cerebro-spinal fluid determines the occurrence of syphilitic meningeal affections of the brain and spinal cord, and possibly also of general paralysis of the insane and tabes dorsalis.

Channels of Toxic Infection.—(*a*) Through the blood. This is the usual mode of infection. Thus, the toxins which produce acute and subacute myelitis are transported in this way. (*b*) Through the cerebro-spinal fluid. (*c*) Along the spinal nerves; there is evidence that infection of the spinal cord may take place in this manner: Homen injected streptococci into the sciatic nerve of the rabbit. Some days after he found the microbes in the spinal roots and the spinal cord; again, after injecting the virus of tetanus and hydrophobia, the transference of the poison to the cord can be checked by dividing the nerves between the seat of inoculation and the cord. Experiments also tend to show that the diphtheria toxin reaches the cord by way of the nerve trunks.

Cerebro-Spinal Fluid.

This is a colourless alkaline fluid of 1006 to 1008 specific gravity. It contains a trace of serum albumin and albumose, and of a substance which reduces Fehling's solution. Under the microscope a few endothelial cells and an occasional leucocyte may be observed.

Pathology.—The fluid may contain blood or pus. There may be an excess of albumin—*e.g.*, tabes and acute

meningitis. Sugar is generally present in acute meningitis, whether tubercular or septic. Various forms of bacteria may be present—*e.g.*, the meningococcus (cerebro-spinal fever), tubercle bacillus (tubercular meningitis), tetanus bacillus, and streptococci, staphylococci, pneumococci (in other varieties of meningitis).

The sediment of the centrifugalized cerebro-spinal fluid does not normally contain more than two to three lymphocytes (small mononucleated), but in certain chronic and subacute affections of the meninges lymphocytosis is observed—*i.e.*, an excess of small lymphocytes, with sometimes a small number of large lymphocytes. In acute infective meningitis a polynuclear leucocytosis is observed. Lymphocytosis is practically always present in tabes dorsalis and general paralysis of the insane.

The pressure of the cerebro-spinal fluid may be increased in acute meningitis (tubercular, cerebro-spinal), cerebral tumour, and uræmia.

DISEASES OF THE KIDNEYS.

Chief Constituents of Normal Urine.

The normal kidney is about 4 inches long, $2\frac{1}{2}$ inches broad, $1\frac{1}{2}$ inches thick, and its weight is about $4\frac{1}{2}$ ounces. The *cortex* constitutes a little less than a third of its substance.

The main function of the kidneys is the excretion of the nitrogenous waste products of the tissues—urea, uric acid, etc. They also eliminate sulphates, chlorides, phosphates, and other salts; these do not represent tissue metabolism, but are simply those contained in the food swallowed. The urea, uric acid, etc., are not manufactured in the kidney from raw material, but pre-exist as such in the blood, and are removed from it by the renal epithelium (chiefly of the convoluted tubules) by a vital process of excretion. The salts and water are passed through the glomeruli by a biophysical process of filtration.

Urotoxins.—The kidneys are also concerned in the elimination, both in health and disease, of a large number of different toxins. Thus, according to Bouchard, normal urine contains: (*a*) a diuretic, (*b*) a narcotic, (*c*) a salivating, (*d*) a pupil-contracting, (*e*) a heat-reducing; (*f*) an organic convulsant, and (*g*) an inorganic convulsant. Anything which interferes with the proper action of the kidneys may cause the retention of one or more of these substances. The toxins of the various in-

fectious diseases are largely excreted in the urine. It is now known, moreover, that a great number of other diseases—*e.g.*, epilepsy, acute manias—are toxic in nature; it follows that their specific toxins must be present in the urine, and it is probable that one day suitable tests will be devised for their detection.

The existence of *an internal secretion* has not been satisfactorily proved, nor has that of secretory nerves, but the kidneys are abundantly supplied with *vaso-motor nerves*.

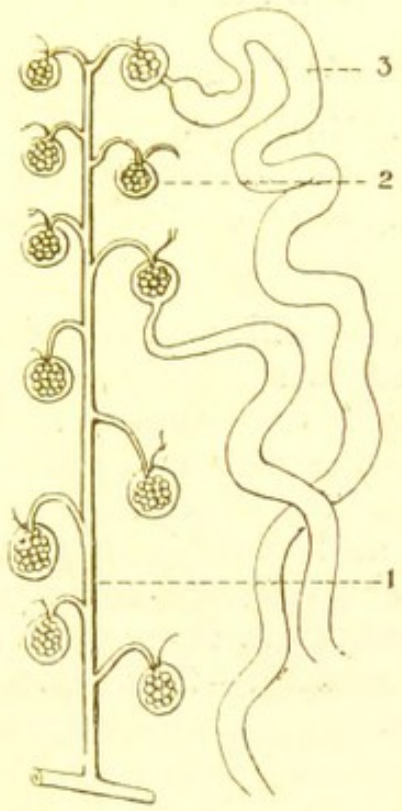

FIG. 13.—CORTEX OF KIDNEY.

1, Interlobular artery; 2, Malpighian body; 3, convoluted tubule.

Dr. Richard Bright in 1827 drew attention to the fact that dropsy and albuminuria are often associated with disease of the kidneys.

Although the term 'Bright's disease' is clinical rather than pathological, it is convenient to use it as synonymous with 'nephritis.'

It is probable that all forms of nephritis (both acute and chronic) are caused by the action of poisons (distinct for each variety) brought by the blood-stream to the kidneys and damaging the renal substance.

These poisons may be absorbed from the oro-alimentary

tube, be derived from bacteria, or they may be products of a vicious metabolism of the tissues. On this hypothesis, quickly-acting poisons cause acute nephritis; slowly-acting poisons, chronic nephritis.

We must suppose that these poisons are especially destructive to the renal epithelium. Possibly the great excretory capacity of the kidneys may lead to an accumulation of such poisons in the renal substance.

There can be little doubt, for example, that scarlatinal nephritis is due to a bacteriogenetic toxin. Vast quantities of the specific toxin are manufactured in scarlet fever, and being eliminated largely by the kidneys, in certain cases the renal substance may be so irritated during the process of excretion that scarlatinal nephritis is set up.

In Bright's disease all the constituent parts of the kidney are involved to a greater or less extent—viz., the glomeruli, the renal epithelium, and the intertubular tissue, although in the different kinds of nephritis these structures are affected in different degrees.

In both acute and chronic nephritis the most conspicuous morbid changes are to be seen in the *cortex* of the kidney, especially in those parts of it where physiological activity is greatest—that is, in the *glomeruli* and *convoluted tubules*.

Acute Nephritis (Parenchymatous, Desquamative).

There are two classical forms of acute nephritis, each varying with the nature of the particular toxin that causes it. In the one form the stress of the inflammation falls more especially upon the tubular epithelium—*tubular nephritis*, and in the other upon the glomeruli—*glomerular nephritis*.

The kidneys become congested and swollen, their capsules being tightly stretched even to the point of rupture. The glomerular vessels may rupture, causing blood to appear in the urine. The epithelial cells, especially those lining the convoluted tubules, swell up, proliferate, and become detached, in some cases choking the tubules. The glomerular tufts may rupture—hence the blood in the urine.

Exudation of inflammatory lymph takes place in the direction of least resistance—*i.e.*, *into the tubules*, which, swelling up and thus being pressed against one another, prevent the exudation of much lymph between them. The intratubular lymph coagulates, and so forms a mould, or *cast*, of the tubule. If the cast consists of a plain mould of the interior of the tubule without any cell elements, it is known as a *hyaline* cast. The detached epithelial cells may adhere to the outside of the coagulum or become intimately mixed with it, thus producing an *epithelial cast*. Later on the shed epithelium may undergo various kinds of degeneration, the result being the formation of *granular*, *fatty*, and other casts.

The damaged tubules allow the escape into the urine of serum albumin and serum globulin of the blood (but never fibrinogen). The casts and shed epithelium tend to block some of the tubules, and this largely explains the scanty urine of acute nephritis.

When recovery sets in, the inflammatory products are in part expelled into the urine and in part absorbed. Some of the tubules are rendered *hors de combat* and atrophy, whilst others, hitherto imperfectly developed, attain full physiological maturity and functionally compensate for those irreparably damaged.

The Large White Kidney.—If recovery does not ensue and the disease becomes chronic, we have the condition known as 'large white kidney.'

The organ is now enlarged (the two kidneys together may weigh 28 ounces, as against 9 ounces in health); the capsule readily strips off, leaving a smooth surface. On section the cortex is seen to be thickened, pale, and mottled; the convoluted tubules are filled with detached epithelial cells in a state of fatty and granular degeneration, fatty and granular casts occupy the straight tubules, and proliferated epithelium is seen within Bowman's capsule. Small embryonic cells, which may later develop into tissue fibres, make their appearance between the tubules.

The patient generally dies at this stage, either from uræmia or some visceral inflammation (pericarditis, pneumonia, pleurisy). If he continues to live, the disease passes into the stage of secondary chronic interstitial

nephritis, allied to granular kidney. Some hold that it may pass into

The Pale Granular Kidney.—In this the cortex may be of normal thickness, or much reduced in size, according to the time the disease has lasted. In a typical case the organ is pale, fibrous, shrunken, and granular on the surface. The fibrous tissue is chiefly intertubular, many of the tubules and glomerular tufts are atrophied, whilst other tubules are blocked with detached epithelial cells.

It is probable, as Dr. Rose Bradford contends, that the pale granular kidney is a chronic disease from the beginning, and not a development from a preceding acute stage.

It is a rare disease, the writer having seen but three cases, all of whom died from acute uræmia within a few months of the development of albuminuric retinitis. Œdema is generally absent, and so the disease is often overlooked until the onset of uræmia or failure of vision. It is manifestly due to the action of a renal poison quite distinct from that causing the red granular contracted kidney.

Red Granular Contracted Kidney (Primary Chronic Interstitial Nephritis, Gouty Kidney).—Red granular contracted kidney is not a sequel to acute nephritis, but is *ab initio* a chronic disease due to the long-continued action of a specific renal poison generated within the organism as the result of faulty metabolism. It is of frequent occurrence after the age of forty, and very insidious in its course, sometimes not being diagnosed until near its fatal termination, which is usually from *cerebral apoplexy* or from *cardiac failure* (dilated left ventricle). The kidneys are small, sometimes remarkably so, Hilton Fagge quoting a case in which the two together weighed under 1½ ounces. The capsules are thickened and adherent, and, when removed, portions of kidney tissue are pulled off with it, the exposed surface showing small granulations, varying in size from $\frac{1}{16}$ to $\frac{1}{8}$ inch. The colour is usually a dark red. On section the cortex is seen to be shrunken, often being reduced to a mere shell of but $\frac{1}{4}$ to $\frac{1}{8}$ inch in thickness; here and there small cysts are present.

The disease may occur secondarily to the long-continued action of such a poison as lead, or in association with gout;

but it often occurs as a primary disease in those leading perfectly healthy lives.

The pathological changes are essentially—

A fibrosis, with
Tubular and glomerular degeneration.

Some hold that the fibrosis constitutes the primary change, the parenchymatous atrophy being secondary to this.

The fibrosis has the following distribution:

(i.) *Periarterial.*
(ii.) *Periglomerular.*
(iii.) *Peritubular.*

(i.) The periarterial fibrosis occurs especially in connection with the cortical arteries. The strands of fibrous tissue around these vessels contract, and this explains the depressions between the granulations on the surface of the organ.

The intrarenal arteries are also themselves considerably thickened, notably their inner coats. The media shows a tendency to atrophy (W. Russell).

(ii.) The capsule of Bowman is greatly thickened, and the entire glomerulus may be converted into a laminated fibrous nodule.

(iii.) The pressure resulting from the contracting intertubular fibrous tissue, coupled with the atrophy of the glomerular capillaries (*vide* ii.), leads to considerable atrophy of the tubules, though it is probable that this atrophy is largely primary, and due to the action of a renal poison.

The cysts in the cortex are caused by the distension of tubules, the channels of which have been constricted by fibroid contraction.

Correlative Pathological Changes in Chronic Nephritis.

When once Bright's disease has become chronic, there occur, with rare exceptions, *cardio-vascular changes.* The left ventricle of the heart becomes hypertrophied, the smaller arteries are thickened by increase in their

muscular and fibrous tissue, and atheroma is often present in the larger arteries, and in those at the base of the brain.

These changes are most characteristically seen in granular kidney. Their pathology in this disease has excited much controversy, and no two authorities appear to agree on the subject. It is, perhaps, somewhat as follows:

In the early stage of granular kidney a substance having a vaso-constrictor action circulates in the blood. What this substance is, or whether it is the one which is responsible for the progressive renal disorganization which characterizes this disease, it is impossible to say; but it is probably not the result of defective renal excretion, seeing that its effects are observed long before the kidneys are seriously disorganized.

The substance in question causes a widespread constriction (hypertonus) of the systemic arterioles, the intrarenal arterioles remaining relaxed. Now, these are the vaso-motor conditions most favourable for diuresis—*i.e.*, an increased pressure in the systemic arteries, including the renal, and a diminution in the resistance offered by the intrarenal arterioles, the conjoint effect being to cause a great augmentation in the pressure, and a corresponding increased rate of blood-flow, within the renal capillaries. In short, the vaso-constrictor substance, which is ever present, brings about just those vaso-motor conditions which are most favourable to its elimination.

It is a mistake to assume, as many writers do, that mere increase in the systemic blood-pressure necessarily increases the urinary flow. A generalized arteriolar constriction, including the renal area, would cause a diminished flow in spite of the augmented blood-pressure. Hence to explain the polyuria of granular kidney we must assume that a generalized arteriolar constriction causing the high blood-pressure is accompanied by a dilatation of the intrarenal arterioles.

The constriction involves the arterioles essentially. It is here that the augmented vascular resistance of Bright's disease resides; the view that it is situated in the capillaries is untenable. Both under physiological and pathological conditions 'peripheral resistance' resides essentially in the region of the arterioles. The writer has shown that the contribution of the capillaries to peri-

pheral resistance is practically negligible. The hypertonus tends, however, to involve the entire systemic arterial tree, the prearteriolar constriction—*i.e.*, of the arteries proximal to the arterioles—being probably of a compensatory nature, tending, as it does, to protect the arteries from the distending effect of the heightened blood-pressure. One of the most important functions of the muscular elements of bloodvessels is by their active constriction to prevent the vessel walls from undergoing a progressive dilatation and elongation. Thus, the radial arteries in granular kidney often feel small, 'tightened up,' and incompressible. These may, however, be large and incompressible, and in such cases the hypertonus, in the upper extremities at least, is limited to the arterioles.

This condition of arterial hypertonus leads to hypertrophy of the media of the hypertonic arteries, and to hypertrophy of the left ventricle, which, owing to the augmented peripheral resistance, has increased work put upon it. On the other hand, the media of the hypotonic intrarenal arteries tends to atrophy (W. Russell).

In the hypertonic arteries the intima and adventitia stand in sharp contrast as regards the influences they are subjected to, for while a hypertonic media protects the enveloping adventitia from the augmented blood-pressure, the intima receives the full brunt of that pressure, as does also the endocardium of the left ventricle. This state of things continuing hour by hour, by day and by night, year after year, it is not surprising that both these structures should undergo some responsive change: briefly, they tend to thicken, while the large arteries and the left ventricle, especially in the region of the valves, become atheromatous.

A further effect of the augmented blood-pressure is that the left ventricle and entire systemic arterial tree tend to dilate, the extent to which they do so depending upon the behaviour of their muscular elements.

So long as the muscular tissue of the heart remains sound, it is capable of effectual systole; but when it degenerates, as in process of time it does, the degenerated muscle fibres being replaced by fibrous tissue, the left ventricle fails to empty itself adequately during systole, an excess of residual blood remains after systole, and

thus by degrees it comes about that the left ventricle, overdistended, during its stretchable phase of diastolic relaxation, by this load of residual blood plus that flowing in from the lungs, becomes unduly stretched, and yields — *i.e., dilates.*

In like manner, the extent to which the arteries become stretched, giving rise to tortuosity and dilatation, depends upon the condition of the muscular media. Let us suppose hypertonus to be maintained fairly generally throughout the arterial tree; it is probable that in such a case little or no permanent yielding will occur until the muscular elements have been to a large extent replaced, as in advanced cases they tend to be, by a hyaline fibroid material. In those arteries, however, which do not become hypertonic, early yielding is likely to occur. Thus, in the cases in which the radial arteries are tightly contracted, these vessels may long remain quite straight and undilated—even, indeed, throughout the entire course of the disease; but in those cases in which the radials tend towards a state of hypotonus, they early become dilated and tortuous. It is probable also that the occurrence or absence of a dilated aorta in granular kidney largely depends upon the degree of tonicity of the vessel.

The adventitia tends to remain unaffected in granular kidney so long as it is protected—*i.e.*, so long as the blood-pressure is borne off from it by a hypertonic media. If the media does not become hypertonic, or if, in process of time, a hypertonic media degenerates, the adventitia yields before the augmented blood-pressure and undergoes compensatory thickening.

Here it may be observed that mere hypotonus of an artery is competent, if persistent, to produce *in a person with habitual low blood-pressure a dilated, tortuous, and thickened vessel.* This may frequently be observed in the temporal arteries, sometimes also in the case of the radial arteries. The relaxed media allows all three coats of the vessel to be stretched to an extent which does not occur normally. As a result the vessel becomes permanently lengthened (tortuous) and dilated, while the strain on the fibrous elements causes hyperplasia of them, the vessel wall thus becoming thickened.

The dilatation, tortuosity, and thickening observed in arteries carrying on collateral circulation are also probably due to relaxation of the media.

Among the other results of the heightened blood-pressure in granular kidney are the formation of miliary aneurisms in the cerebral arteries, granular kidney being *par excellence* the cause of cerebral apoplexy.

In chronic Bright's disease, and especially in granular contracted kidney, there is a marked tendency to *hæmorrhage*. As Hale White puts it : '*A person with Bright's disease may bleed from anywhere—e.g.*, from the brain, retina, lobe of the ear, nose, lungs, alimentary and urinary tracts.'

Patients with granular kidney generally have emphysematous lungs.

Pleurisy, pericarditis, and pneumonia are common complications of Bright's disease, whether acute or chronic.

Albuminuric retinitis is met with in the chronic forms of renal disease alone, and occurs in about 28 per cent. of the cases. The prognosis is very unfavourable, most of the patients dying within a few months of the first appearance of retinal changes.

Scarlatinal Nephritis.

In this form of Bright's disease the general phenomena are the same as those described under acute nephritis, but there are some special points to be mentioned in connection with it. The scarlatinal poison has a special affinity for the Malpighian bodies and the small arteries connected therewith. The intima of these arterioles, particularly that of the afferent vessels of the glomeruli, undergoes hyaline degeneration. Bowman's capsule is swollen, and the cells of its epithelial lining proliferate, in some cases to such a degree as almost to fill up its interior, and, by compressing the glomerular tuft, to cause its atrophy.

Should the disease become chronic, by one to three years' time, the whole Malpighian body may be seen to be composed of concentric laminæ of fibrous tissue, with complete obliteration of the glomerular vessels. The branches of the renal artery become thickened from chronic endarteritis and periarteritis.

Tuberculosis of Kidney.

This is usually a disease of early adult life, and in the large majority of cases is primary—due, *i.e.*, to *infection through the blood-stream*. It is unilateral in 92 per cent.

of cases (Krönlein). Sometimes it is associated with tuberculosis of the epididymis, the vas deferens, the vesiculæ seminales, and the trigone of the bladder.

It may begin in any part of the organ, but more commonly starts near the apices of the papillæ, spreading thence into the kidney, on the one hand, and into the calices, pelvis, and ureter on the other. Caseation and ulceration take place, and the curdy pus and necrotic débris thus resulting are expelled with the urine. If at this stage the interior of the bladder be viewed with the cystoscope, the opening of the ureter is seen to be everted and to 'pout,' and the urine trickling from it to be turbid.

If the thickened and contracted ureter becomes blocked by the caseous material, *pyonephrosis* results, and this in turn may be complicated by the formation of a *perinephritic abscess* in the loin. In many cases the urine contains, in addition to the tubercle bacillus, the *Bacillus coli*, the staphylococcus, and the streptococcus.

At the post-mortem examination of an advanced case the following changes are found: The kidney is greatly enlarged; the perinephritic fat, thickened by chronic inflammation, is adherent to the capsule; the cortex is represented by a toughened shell; the medulla and papillæ have disappeared; the pelvis is dilated; its walls are thickened, and its interior may present a characteristic 'mouse-nibbled' appearance. The dilated cavity is filled with a curdy pus, which in some cases is transformed into a putty-like mass. The ureter is adherent to the neighbouring parts; its walls are infiltrated with tubercles, and its lumen is contracted.

Transitory Nephritis.

In the albuminuria of pneumonia, enterica, diphtheria, and other febrile disorders, a toxin must in some way damage the tubules, allowing the escape of the albuminous constituents of the blood. When this happens, the condition is known as transitory nephritis.

The ingestion of turpentine, cantharides, mercury, and other poisons, may also cause albuminuria. Cantharides in some cases induces a marked glomerular nephritis, in many respects resembling scarlatinal nephritis.

In acute alcoholism temporary albuminuria is common.

In *secondary syphilis* there may be albuminuria, due, probably,

to an injury inflicted on the renal epithelium by the specific toxin.

In *tertiary syphilis* there may be either a diffuse gummatous infiltration of the kidneys, or the development in them of definite gummata (as in the case of the liver). The urine in these syphilitic cases may contain abundant albumin, yet dropsy and the other symptoms of Bright's disease may be absent.

Congenital Cystic Disease.

In this condition the kidneys are greatly enlarged and converted into a mass of cysts, suggesting in appearance a bunch of grapes. The cysts, separated by the remains of the renal tissue, are lined with epithelium, and contain an albuminous fluid. The proper kidney substance is atrophied. The disease has been attributed to some anomaly in development, or to an inflammation of the papillæ, causing occlusion of the ducts.

A similar condition is sometimes, but very rarely, met with in adults. In this form also the kidneys are greatly enlarged, and may weigh from 1 to 6 pounds.

Hydronephrosis.

Hydronephrosis is the condition in which the kidney is converted, partially or entirely, into a cyst, as the result of some obstruction to the urinary outflow. The pelvis and the calices undergo dilatation; the medulla becomes atrophied, the process of atrophy starting at the papillæ and spreading outwards; and ultimately the kidney is transformed into a mere cyst, which may be either small or of considerable size. The condition may be congenital or acquired, and, according as the obstruction affects one or both sides, unilateral or bilateral.

The congenital causes are developmental abnormalities of the ureter and imperforate urethra; the causes in later life are such conditions as the presence of a calculus in the ureter, cicatricial contraction of the ureter, pressure on the ureter by a growth (*e.g.*, carcinoma of the uterus), enlarged prostate, and stricture of the urethra.

Tumours of the Kidney.

These are rare. A peculiar form of sarcoma, called *rhabdosarcoma*, owing to the admixture of striated muscle fibres, is sometimes found in infants. (It is noteworthy in this connection that both kidneys and muscles are developed from the mesoblast.) Other tumours of the kidneys are adenoma, sarcoma, and carcinoma. Sarcoma is the most frequent malignant tumour, and generally occurs in children.

DISEASES OF THE LIVER.

Average weight in adult=50 to 60 ounces, being one-fortieth of the body-weight. At birth=one-twentieth of body-weight.

The liver is developed as a diverticulum of the primitive gut. The liver cells are hypoblastic, and the stroma is mesoblastic in origin. The organ is composed of lobules, each of which is about $\frac{1}{16}$ inch in diameter. Between the lobules is a supporting connective tissue carrying the lymphatics, bloodvessels, and bile-ducts. Within the lobules are the liver cells, closely packed, in form polyhedral from mutual pressure, and separated from one another by a sparse and very delicate tissue, continuous with the interlobular connective tissue. The portal vein drains the blood from the capillaries of the whole of the alimentary mucous membrane, between the lower end of the œsophagus and the lower end of the rectum. It terminates in the capillaries of the liver lobules, where a junction is effected with the capillaries of the hepatic artery.

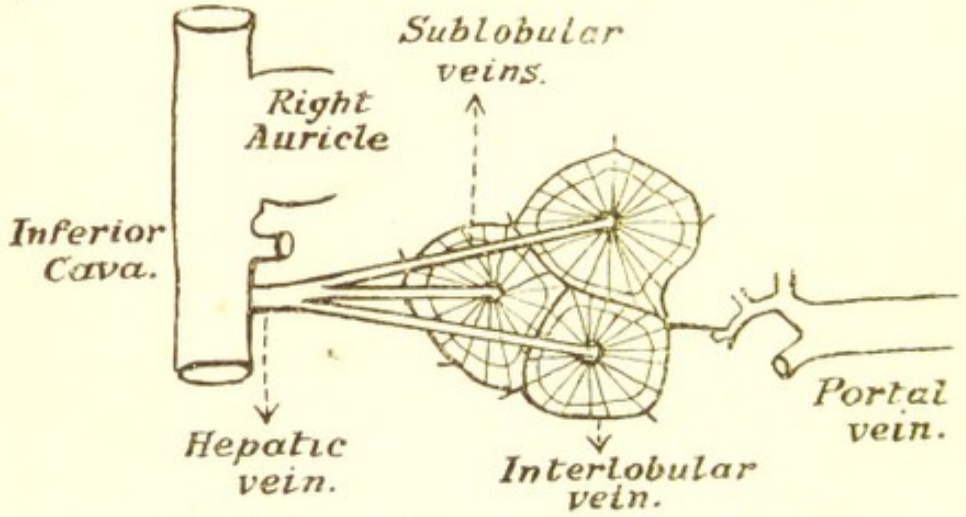

FIG. 14.—DIAGRAM SHOWING CIRCULATION OF THE PORTAL BLOOD THROUGH THE LIVER.

The portal vein is seen to divide and subdivide, and to break up into the interlobular veins which run between the hepatic lobules. From the interlobular veins capillaries (portal) pass to the intralobular veins. These are gathered up into the sublobular which enter the hepatic veins (of which there are several), which again open into the inferior cava. The intralobular branches of the hepatic arteries form capillaries, which unite with the portal capillaries.

The blood is carried *from* the liver lobules by the *hepatic system of veins*, and thence to the right heart. The portal circulation is peculiar in that it begins and ends

in capillaries, and is destitute of valves. All the substances absorbed from the gastro-intestinal tube, with the exception of most of the fat, pass into the portal system, and have to be subjected to the influence of the liver before they can enter the general circulation.

The liver is the great biochemical laboratory of the body. It normally reduces many nitrogenous waste products to substances —*e.g.*, urea, uric acid—which the kidneys excrete; it destroys ptomaines and other poisonous bodies, and *is the great detoxinator or blood-purifier*. Interference with these functions leads to auto-intoxication and impairment of the general health.

Jaundice.

Jaundice is a condition in which the bile enters the general circulation, and stains the fluids and tissues of the body yellow. The view now held is that it is *in all cases caused by some obstruction to the outflow of bile into the duodenum*, in consequence of which it is first absorbed by the lymphatics of the liver, and thence passes into the blood-stream through the lymphatic duct. *Ligature of the thoracic duct prevents jaundice.*

The obstruction may arise from (*a*) causes acting within the lumen of the ducts (gall-stones); (*b*) causes primarily involving the duct walls (catarrh of the mucous lining); (*c*) pressure from without (tumours—especially malignant disease of the liver or pancreas — and hypertrophic cirrhosis).

For pathological purposes the liver lobule may be divided into three zones. Fatty degeneration begins in the outer zone, amyloid disease in the intermediate zone, and 'nutmeg' liver in the central zone.

Fatty Degeneration.

The organ is enlarged, light brown, and in advanced cases even yellow in colour; on section it presents a greasy appearance. In the slighter cases the fat globules are limited to the cells of the peripheral zone; in fully developed cases the fatty degeneration affects all the cells of the lobule. The liver may become markedly fatty in phthisis, chronic alcoholism, phosphorus, arsenic, or chloroform poisoning, in pernicious anæmia, and all other

forms of severe anæmia. Cloudy swelling is liable to pass into fatty degeneration; hence fatty degeneration of the liver may be found in diphtheria and all other acute infections.

Lardaceous, or Waxy, Liver.

The organ is much enlarged—even to three times its normal size—and though its general contour is preserved, the edges become thick and rounded, and the whole mass is so compact that it cuts like raw bacon. The cut surface has a waxy appearance: hence the name. The neighbouring liver cells are often atrophied, and fatty degeneration is common. A weak solution of iodine renders the amyloid material mahogany-brown, while gentian violet stains it a deep rose-pink and the normal tissues blue.

The change begins in the intermediate zone.

The disease is always associated with lardaceous degeneration of the spleen and kidneys.

Chronic Venous Congestion ('Nutmeg Liver').

This condition is caused by obstruction to the free flow of the blood from the hepatic veins, as the result either of heart disease, or of primary obstruction in the pulmonary circuit—*e.g.*, emphysema of the lungs, or fibroid phthisis.

A fact to bear in mind in connection with this disease is that no valves intervene between the central intralobular hepatic veins and the right heart. Thus, when compensation fails—*e.g.*, mitral regurgitation—the 'backwash' from the left heart will produce its effects first on the lungs, then on the right heart, and then very readily on the valveless hepatic veins.

Course of the Disease.—The central intralobular vein becomes much distended and thickened, and the capillaries opening into it become dilated and tortuous. The liver cells atrophy from the centre of the lobule outwards. The central zone of the lobule becomes pigmented (the pigment being derived either from the blood or the bile), while at the periphery of the lobule the cells tend to undergo fatty degeneration, so that on section there is seen a dark inner zone alternating with a pale peripheral one.

Hence the liver presents a marbled, or 'nutmeg,' appearance.

Sooner or later some fibrosis occurs, first in the centre and then at the periphery of the lobules.

In advanced cases the cells of the inner zone are completely destroyed.

In the early stages the liver is enlarged as the result of the mechanical congestion; later on it becomes smaller from atrophy of the liver cells, and the capsule undergoes thickening, and may present a wrinkled appearance.

On section much blood may gush out; on washing the surface the characteristic 'nutmeg' appearance is displayed.

Abscess of the Liver.

Abscess of the Liver is always due to infection by micro-organisms. The two principal types are the *Pyæmic* and the *Tropical*.

Pyæmic Abscesses.—In ordinary pyæmia abscesses rarely occur in the liver, the more usual sites being the lungs and the joints. When pyæmic abscesses do involve the liver they are small and multiple, and contain a putrid yellow pus.

In *suppurative pylephlebitis* (*'portal pyæmia'*) the infection comes from some part drained by the portal system of veins, generally from an ulcerated portion of the alimentary tube; abscesses may also follow operations for hæmorrhoids. They are small and numerous, and lie in the course of the distribution of the portal vein, the branches of which are seen to be filled with puriform clots.

Tropical Abscess.—This disease is due to infection by the *Entamœba histolytica*, conveyed by the portal circulation, and in the majority of cases is secondary to a dysentery owning the same cause. Alcohol is probably the most important 'soil preparer.' The pus is of a slimy, gummy consistence, of chocolate colour, and composed of necrosed and liquefied liver cells, with an admixture of blood, ordinary pus cells being either few or absent. *It is sterile*, no cultures of bacteria being obtainable by the ordinary methods. As pointed out by Manson, the entamœbæ are numerous in the spreading margin of

the abscess, and though absent in the pus when first drawn off, they make their appearance in the discharge about three days later—that is, when the walls of the abscess begin to granulate and to contract.

The abscess is generally situated deep in the right lobe, and may contain several pints of fluid. After a time the pus tends to make its way to the surface of the liver, causing adhesions to neighbouring structures; and if the condition is untreated, the pus ultimately escapes into the pleura, lung, peritoneum, or externally through the abdominal walls, and in rarer cases into the stomach, gall-bladder, hepatic duct, portal vein, inferior vena cava, pelvis of right kidney, pericardium, or other parts.

Occasionally the abscess becomes surrounded by a thick fibrous capsule.

In rare instances abscesses in the liver are caused by a *suppurating hydatid*, and by the *Streptothrix actinomyces*.

Subphrenic Abscess.

Owing to the cruciform arrangement of the falciform, coronary, and lateral ligaments of the liver, there are six possible situations which a subphrenic abscess may occupy — four intraperitoneal and two extraperitoneal (between the layers of the coronary ligament). The following table (taken from Barnard's 'Contributions to Abdominal Surgery') gives the position in seventy-two cases:

	Gastric Ulcer.	Appendicitis.	Hepatic Abscess.	Duodenal Ulcer.
Intraperitoneal, right anterior	4	10	7	1
Intraperitoneal, right posterior	1	6	1	2
Intraperitoneal, left anterior	16	1	1	1
Intraperitoneal, left posterior	2	0	0	0
Extraperitoneal, right	0	1	15	2
Extraperitoneal, left	1	0	0	0

Cirrhosis of the Liver.

Of this disease there are three classical forms. The cause in each would appear to be some irritant, probably

toxic in nature, present in the liver, and brought there—

By the portal blood (alcoholic cirrhosis);
By the bile-ducts (hypertrophic cirrhosis); or
By the general circulation (syphilitic cirrhosis).

Alcoholic Cirrhosis ('**Hobnail Liver**,' '**Gin-drinker's Liver**,' **Chronic Interstitial Hepatitis, Atrophic Cirrhosis**).—The essential pathological change in this disease is an increase in the connective tissue *around the interlobular branches of the portal vein.* An irritant, circulating in the portal blood, first starts a *periphlebitis;* there then occurs a small round-celled infiltration, which ultimately becomes organized into fibrous tissue. This tissue tends to surround groups of several lobules rather than to envelop each individual lobule. In course of time the new tissue contracts and strangles the branches of the portal vein within the liver, and as a consequence there results great distension of the portal radicles in the gastro-intestinal tract and mesentery; hence ensue hæmatemesis, melæna, ascites, and enlarged spleen.

According to some pathologists, the irritant primarily acts upon the liver cells, causing their atrophy, the growth of the connective tissue being a secondary phenomenon.

The irritant which provokes the cirrhosis consists either of the alcohol itself, impurities in the alcohol, or of certain toxins liberated in the alimentary canal as the result of chronic gastro-intestinal catarrh caused by alcoholic excess.

'When we consider that cirrhosis is found in horses in Switzerland and in cattle in Nova Scotia; that it is common among abstaining Hindoos, who live on highly spiced foods; and that it attacks the Fuegians, who develop a severe form of it, and whose staple diet consists of large quantities of mussels, good and bad, with their abundant nitrogenous elements, it will be seen that the only factor common to all is the gastro-enteric tract, with its liability to irritation and putrefactive change' (Stenhouse and Ferguson).

The cirrhotic liver varies considerably in size, according to the stage the disease has reached. The organ is always enlarged at first, sometimes to more than twice its normal size; on the other hand, it may subsequently be

reduced to less than half its normal size. At the time of death in about 50 per cent. of cases it is enlarged, and in the other 50 per cent. contracted.

As seen in the post-mortem room, the typical cirrhotic liver presents the following appearances: Its surface is irregular, being marked by elevations which suggest the hobnails of a boot ('hobnailed' liver), and often by large round bosses as well. The capsule is usually thickened, and adherent to the surrounding peritoneum. On section the organ shows bands of fibrous tissue, which form a network throughout the liver substance, dividing it into 'islands' of various sizes, each of which contains separate groups of lobules: hence the name of 'polylobular' cirrhosis. The fibrous bands from the interior can be traced to the peritoneal surface, where they are seen to pass to the depressions between the 'hobnails.' The 'hobnails,' in fact, are portions of liver substance which have been thrust outwards by the contraction of these fibrous bands.

The new tissue consists of round cells, delicate spindle cells (fibroblasts), and wavy bundles of fibrous tissue, the relative proportions of which vary with the duration of the process.

In the fibrous bands are numbers of new-formed blood-vessels, which anastomose with the branches of the hepatic artery. In some cases double rows of cubical cells are seen, suggesting a new formation of bile-ducts, but the significance of these is still doubtful. The liver cells undergo atrophy, and in beer-drinkers fatty degeneration of the peripheral zone of the lobule is common. When the atrophy of the cells is advanced, toxic symptoms supervene not unlike those which occur in acute yellow atrophy.

The collateral vessels between the portal and systemic veins become dilated, and thus relieve the congestion of the portal area. This compensatory anastomosis is carried out principally between the following sets of veins: The œsophageal and gastric; the epigastric and internal mammary; the inferior mesenteric and hæmorrhoidal branches of the internal iliac; the portal branches in the round ligament of the liver, and the epigastric and internal mammary at the umbilicus (caput Medusæ); branches of the portal vein in the mesentery, with the inferior vena cava and its branches (veins of Retzius).

Hypertrophic or Biliary Cirrhosis (Hanot's Disease).—In this comparatively rare disease the liver is greatly enlarged, firm, and smooth. The newly-formed connective tissue is more delicate than in the other kinds of cirrhosis, and it *surrounds each individual lobule;* hence the name of 'unilobular' cirrhosis applied to it by Charcot.

In the new tissue are enormous numbers of so-called bile-capillaries. As there is no obstruction to the portal circulation, hæmatemesis, melæna, and ascites are not present, unless there is an associated portal cirrhosis. Jaundice, on the other hand, is a constant feature.

The cause is unknown. The theory has been advanced that it is due to a microbic infection of the bile-ducts from the duodenum, causing retention within the liver of bile, which, in conjunction with the infecting agent, irritates the liver tissue.

Obstructive Biliary Cirrhosis.—In certain cases of biliary obstruction, such as those due to impacted calculus, cancer of the liver or pancreas, an interlobular cirrhosis is met with, associated with dilated bile-ducts, and the formation of what look like bile-capillaries, but which probably consist simply of double columns of altered liver cells.

Syphilitic Cirrhosis—*Congenital Syphilis.*—In infants dying three or four months after birth it is not uncommon to find an interlobular cirrhosis uniformly affecting the whole liver. In many cases the new tissue *penetrates into the lobules, and so becomes pericellular.* The liver cells are degenerated. Gummata may also be present.

Acquired Syphilis.—In this disease the liver may become infiltrated with a diffuse gummatous material, which by organizing causes it to be seamed with fibrous bands.

Definite gummata may also occur, but these are always connected with a preceding syphilitic cirrhosis. The gummata form pale yellow, well-defined, rounded masses, generally springing from the surface, which is often adherent to the neighbouring structures, such as the diaphragm. They are surrounded by a fibrous capsule. When fresh, they may be soft and pulpy; later, they may become hard, like cartilage.

The Drunkard's Liver.

This subject has given rise to much confusion, some authorities maintaining that the liver is enlarged, and others that it is contracted. As ordinarily seen in the out-patients' department of a London hospital, it is certainly *enlarged*, and often very much so. This enlargement is probably the resultant of three distinct pathological conditions:

(*a*) *Blood and lymph engorgement;*
(*b*) *Fatty infiltration and fatty degeneration;*
(*c*) *A small embryonal-celled infiltration.*

A drunkard usually dies from pneumonia, or fatty degeneration of the heart, before (*c*) can organize into connective tissue and contract.

Banti's Disease.

In this rare disease there is a combination of hepatic cirrhosis with splenic anæmia.

Tuberculosis of the Liver.

Tubercles form both beneath the capsule and in the interior of the liver. By coalescence they may attain the size of a hazel-nut (rare). Sometimes they develop along the walls of the hepatic ducts, and, by compressing them, cause jaundice (very rare).

Tumours of the Liver.

Cavernous Angioma is the commonest of the non-malignant tumours of the liver. It may range in size from a pea to an orange.

Adenomata are very rare. They occur in the form of nodules, composed of acini lined with cubical epithelium.

Primary Sarcomata are also very rare. Secondary sarcomata, particularly the melanotic variety, sometimes form in the liver.

Primary Carcinoma is rare, constituting only about 4 per cent. of hepatic cancers.

Secondary Carcinoma is common; indeed, it is the only hepatic tumour which is at all common. 'Of all persons in whom at death malignant disease of any organ is found, about 50 per cent. have secondary deposits in the liver' (Hale White). The primary growth may be situated in any part of the body, but its usual seats are the gastro-intestinal tract, the head of the pancreas, the gall-bladder, and the uterus. The hepatic tumours are usually multiple; the superficial ones often present an umbilicated appearance from breaking down of their central parts. Owing, it is supposed, to the great vascularity of the liver, they grow quickly, the duration of life being seldom more than eight months after the first recognition of the disease. Hæmorrhage into the interior of the tumours often takes place. The heaviest livers on record have been cancerous.

Acute Yellow Atrophy.

This is a very rare disease (not more than 300 cases on record). It is probably toxic in nature, due to the action of a *hepato-lysin—i.e.*, a substance capable of dissolving the liver cells (see p. 38). It causes so rapid an atrophy of the liver that in the course of a few days it may be reduced to half its original bulk. The malady is commonest in women, usually occurring in connection with pregnancy.

As seen after death, the liver is much shrunken. No longer preserving its normal shape, it flattens out when placed upon the table, lying loose in its wrinkled capsule (like a half-filled bag). On section the surface presents a bright yellow colour—hence the name—the outlines of the lobules are indistinct, and the liver cells are for the most part broken down and replaced by a granular débris, though here and there clumps of comparatively healthy cells are to be seen.

The disease bears a close resemblance to phosphorus-poisoning. As Vivian Poore pointed out, it is found in young pregnant prostitutes who have committed suicide by phosphorus-poisoning, and according to him many alleged cases of acute yellow atrophy have been in reality cases of phosphorus-poisoning.

Enlargements of the Liver.

Regular=nutmeg liver, fatty infiltration, lardaceous disease, biliary cirrhosis, polylobular cirrhosis (early stage), leukæmia, lymphadenoma, diffuse cancerous infiltration, portal pyæmia.

Irregular=malignant growths (secondary), hydatid, abscess, gummata.

DISEASES OF THE GALL-BLADDER AND BILE-DUCTS.

Inflammations of the gall-bladder are termed *cholecystitis*, and of the bile-ducts, *cholangitis;* they are chiefly due to microbic infection travelling up from the duodenum, the infective agent often being the *Bacillus coli* and the *Bacillus typhosus*. If cholecystitis be suppurative, the condition is known as *empyema of the gall-bladder*. In such cases there is generally impaction of the cystic duct by a gall-stone.

In old-standing cases of cholecystitis the gall-bladder is usually much thickened and contracted, being drawn up and buried under the liver, and adherent to the surrounding parts.

Carcinoma of the gall-bladder when found is almost invariably associated with gall-stones.

Gall-Stones (Cholelithiasis).

Gall-stones are concretions consisting chiefly of cholesterin, with an admixture of bile-salts and bile-pigment. (Cholesterin is excreted by the mucous membrane of the gall-bladder.) Often they contain a small quantity of calcium salts, but insufficient in amount to throw a definite shadow with the X rays. Most frequently they are formed in the gall-bladder, even when found in the hepatic ducts; in rare instances, however, they may form primarily in the ducts. Gall-stones vary in size from small grains of sand to masses as large as a walnut. They are often multiple, and as many as 7,802 (Otto) have been found in the gall-bladder. If multiple, they often present smooth, flat facets from mutual friction. When dry, the calculi

float in water; otherwise they sink. They are most common in women over forty.

The first stage in the production of gall-stones would appear to be an antecedent catarrh *of a specific kind* of the gall-bladder, or bile-ducts, from microbic infection. As the result of such catarrh the epithelium becomes shed, and, acting in conjunction with the infecting agent, forms a nucleus round which the hard matter is deposited.

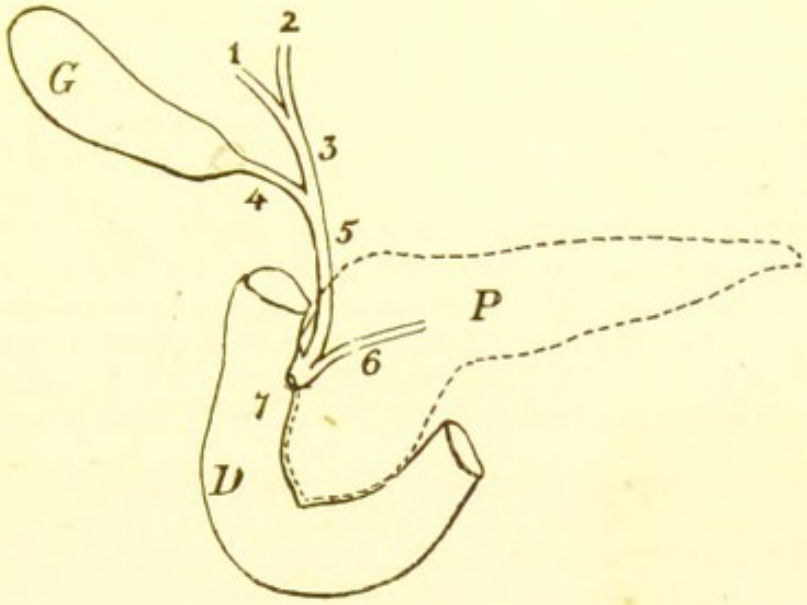

FIG. 15.

1 and 2, Right and left hepatic ducts; 3, the hepatic duct; 4, the cystic duct; 5, the common bile-duct; 6, the duct of the pancreas; 7, the ampulla and papilla of Vater.

In other cases the bacteria themselves may form the nucleus.

Complications:

Obstructive jaundice.
Empyema of the gall-bladder.
Ulceration into duodenum (intestinal obstruction).
Ulceration into hepatic flexure of colon.
Carcinoma of gall-bladder.
Stenosis of the common duct.
Cirrhotic changes in liver and pancreas.
Subphrenic abscess.

DISEASES OF THE PANCREAS.

Acute Pancreatitis.—This is always due to bacterial infection, usually from the duodenum (*vide* Fig. 15). Gall-stones, by fretting the epithelial lining of the terminal part of the duct, strongly predispose to it. There are three chief forms, each of which probably owns a different infecting agent:

Acute Hæmorrhagic Pancreatitis.—In this disease the greater portion, if not the whole, of the gland becomes infiltrated with blood, and its cells undergo necrosis. There may also be fat necrosis in the pancreas, omentum, and elsewhere.

Suppurative Pancreatitis. — This is characterized by the presence of either a single abscess or of small multiple ones.

Gangrenous Pancreatitis. — This may affect a part or the whole of the gland, the tissue being converted into a dark slate-coloured mass.

In **Chronic Pancreatitis** there is an overgrowth of the fibrous tissue of the organ, with atrophy of the glandular elements. In extreme cases the condition is known as *cirrhosis of the pancreas.* The usual cause is obstruction to the outflow of the pancreatic juice, arising from the lodgment of a gall-stone in the terminal part of the common bile-duct.

Tumours of the Pancreas.

Pancreatic Cysts may be of several kinds: *Retention cysts*, which may be as big as a child's head, result from obstruction to the outflow of the pancreatic secretion—*e.g.*, from impacted calculus or pressure, from without, as from chronic pancreatitis; *cysts in connection with growths* — *e.g.*, adenoma, carcinoma; *hæmorrhagic cysts; hydatid cysts.*

Adenomata may occur, but they are extremely rare.

Carcinoma usually affects the head of the pancreas. Some of the cases start in the neighbouring glands, and involve the pancreas secondarily.

Pancreatic Calculi are sometimes met with. They consist principally of calcium carbonate, and they may cause obstruction in any part of the main pancreatic duct. They are usually multiple.

DIABETES MELLITUS.

Diabetes is a clinical term, and is used in a generic sense, like jaundice, to indicate a symptom—*i e.*, persistent glycosuria.

The sugar which appears in the urine is *dextrose* ($C_6H_{12}O_6$).

Normal urine contains dextrose, but in insufficient quantity to give the ordinary reaction with Fehling's solution. (Uric acid, kreatinin, glycuronic acid, alkaptonuria, lactose, pentose, lævulose, all reduce Fehling's solution.)

Experimentally, diabetes can be induced in animals by any of the following methods :

Puncturing the floor of the fourth ventricle.
Removing the pancreas.
Administering phloridzin.
Administering adrenalin.
Administering thyroid extract.

Puncturing the Floor of the Fourth Ventricle.—Diabetes thus induced is thought to be due to damage of a centre in the medulla which controls the glycogenic action of the liver cells.

'There are experiments recorded which show that the liver nerves have a direct influence on the liver cells, quite apart from their influence on the bloodvessels' (Halliburton); in other words, that the liver is provided with 'trophic' nerves.

Removing the Pancreas.—Removal of the entire pancreas in animals causes severe and fatal glycosuria; if, however, even a very small portion of the gland is left behind, glycosuria does not ensue. The glycosuria thus induced has been ascribed to the loss of the internal pancreatic secretion, which is assumed to influence the carbohydrate metabolism of the tissues.

'The "islets of Langerhans" have probably nothing specifically to do with the production of this internal secretion, for it has recently been shown that the islets are only phases in the life-history of the ordinary secreting acini' (Halliburton).

Administering Phloridzin.—By the administration of this glucoside a very severe form of diabetes is induced, characterized by the presence of abundant sugar in the urine, though the blood contains no more than the normal quantity; it is *glycosuria without glycæmia*, the sugar being formed in the kidney by some substance brought to it by the blood.

'If the phloridzin is directly injected into one renal artery sugar rapidly appears in the secretion of that kidney, and, later, in that of the other kidney' (Halliburton).

Administering Adrenalin.—In the diabetes thus induced there is both *glycæmia and glycosuria.*

Administering Thyroid Extract. — Glycosuria is occasionally noticed after the administration of thyroid extract. (Glycosuria also sometimes occurs in exophthalmic goitre.)

Pathological.—As regards the causal pathology of clinical diabetes, the only fact definitely known is that in a certain proportion of cases the pancreas, post mortem, is found to be diseased. Probably, however, it is only the severer forms of diabetes—*i.e.*, those associated with rapid wasting, great thirst, and abundant glycosuria—which can be ascribed to disease of this organ.

In these cases the pathological changes found in the pancreas consist of an *increase of the connective-tissue stroma, accompanied by atrophy of the parenchyma.*

Glycosuria is uncommon in carcinoma of the pancreas, the reason being that the growth rarely destroys the entire gland.

Diabetic Coma.—The occurrence of this symptom is probably due to the presence in the blood of the fatty acid, *β-hydroxybutyric acid*, which originates from the fat in the body. Both acetone and aceto-acetic acid (derivatives of β-hydroxybutyric acid) are usually present in the urine of patients in whom diabetic coma is impending, but that they are not the actual cause of the coma is proved by the fact that, when they are artificially introduced into the blood, no narcosis results.

'The β-hydroxybutyric acid formed in diabetes is, by oxidation, partly converted into aceto-acetic acid, and, in the urine, this loses carbonic dioxide, and so is partly converted into acetone' (Halliburton).

β-hydroxybutyric acid is probably a normal product of fat metabolism, but whereas in health it is oxidized into carbonic acid and water, in diabetes this oxidation is not effected.

Diabetic Gangrene.—This takes place chiefly in elderly diabetics (about the age of sixty), and it is often the first indication of the existence of diabetes. Its exciting cause is commonly a slight injury, such as may result from

wearing tight boots, or pressure on a corn. Its most frequent site is the foot. There are two chief types—

Mummification.
Perforating ulcer.

Mummification.—The toes become cold and discoloured, and in course of time mummified. They may now be cast off, the parts healing up. In other cases the gangrene extends to the dorsum of the foot.

Perforating Ulcer.—In this form the disease usually starts in the ball of the great toe, often around a corn. The corn suppurates and leaves a painless ulcer, having steep edges, bordered by heaped-up and thickened epidermis, a condition very similar to that sometimes met with in tabes dorsalis. A dusky purple areola soon surrounds the ulcer, which in time becomes gangrenous; the gangrene slowly spreads along the foot until it may even extend as far as the calf of the leg. Whilst confined to the foot it usually remains 'dry,' but once it invades the soft tissues of the calf it tends to become 'moist,' and may at any time lead to septic infection.

In all cases of diabetic gangrene the arteries supplying the part are diseased, the endothelium being greatly thickened and the arterial channels reduced in size, or even obliterated.

DISEASES OF THE DUCTLESS GLANDS.

Diseases of the Thyroid Gland.

The thyroid is a ductless gland, composed of acini lined with cubical epithelium, and filled with the so-called colloid material, which contains a proteid—*thyroiodine*—remarkable for the presence in it of iodine. In fact, the gland contains far more iodine than any other organ in the body, and the activity of the colloid material varies with the percentage of iodine. The stroma is abundantly supplied both with bloodvessels and lymphatics. The gland is developed from the pharynx, and in fœtal life is a compound tubular gland, having a duct—the thyro-glossal—which opens into the foramen cæcum of the tongue. The occasional persistence of this duct explains many of the cysts which develop in the middle line of the neck.

Pathological and experimental observations point to the fact that the thyroid gland elaborates a secretion which exerts an

important influence on the development and nutrition of the whole body, and contains a *vaso-dilator* substance.

The gland attains its full development at puberty, and tends to atrophy in old age.

Goitre (Bronchocele).

Goitre is a clinical rather than a pathological term, and embraces all enlargements of the thyroid gland of non neoplasmic origin.

Classification { Parenchymatous { Cystic. / Fibrous. / Exophthalmic.

Parenchymatous Goitre consists of an overgrowth of the acini of the gland, and to some extent of the stroma. The acini may become cystic ('cystic' goitre), or the stroma may be abundant ('fibrous' goitre). It is usually bilateral. The colloid material is very deficient in iodine, and the chief cause of the disease is probably the deprivation of iodine.

Exophthalmic Goitre is largely *a reversion to the fœtal state*, being characterized by three sets of changes:

(*a*) Alteration in the alveoli.
(*b*) Increase in the connective-tissue stroma.
(*c*) Dilatation of the bloodvessels.

(*a*) The cubical epithelial cells lining the acini become cylindrical. New acini are formed by diverticula from old ones. The *colloid* material becomes more fluid.

(*b*) In the newly-formed connective tissue of the stroma nodules of lymphoid tissue are often found.

(*c*) The bloodvessels (more particularly the veins) become greatly distended and their walls friable, so that during an operation on the gland hæmorrhage is apt to be copious.

The Blood.—The polymorphonuclears are reduced, and the small lymphocytes increased in number.

The *Thymus Gland* is frequently persistent, and the fatty *marrow* of the bones is usually transformed into red marrow.

The most probable explanation of the symptoms of exophthalmic goitre is that they result from an excessive formation of the normal, or the formation of an abnormal,

secretion, which increases the katabolism of the tissues, causing an increased output of carbonic acid and urea, together with loss of weight. Most of the characteristic symptoms—the emaciation, the sweating, the pigmentation of the skin, the tachycardia, the nervous agitation—are referable to this augmented katabolism.

The disease occurs eleven times more frequently in women than in men (Murray). Of hospital patients, 36 per cent. recover under medical treatment.

Tumours.—*Adenoma* of the thyroid is characterized by the formation of large acini, which are enclosed within a distinct capsule separating them from the rest of the gland. In some cases the acini are converted into *cysts* containing a thin brownish fluid. It is generally unilateral.

As the thyroid gland contains both mesoblastic and hypoblastic elements, *sarcomata* and *carcinomata* may occur, but they are extremely rare.

Cretinism and Myxœdema.

It is now recognized that both these diseases depend upon atrophy of the thyroid, and diminution, or entire absence, of its secretion.

Cretinism is a physical and mental defect of development associated with a congenitally defective thyroid. The gland may be either smaller or larger than normal, but in all cases the acini are ill developed.

The symptoms are rarely noticed until the child has reached the age of six months. The teeth erupt late, walking and talking are long delayed, and by the time adult life is reached the cretin may be mentally and physically as undeveloped as a child of five.

The head in cretins is large and broad, the hair coarse, the nose flat; the eyes are widely separated, the lips greatly thickened, as is also the tongue, which usually protrudes from the mouth. The skin is coarse and rough. The abdomen is pendulous, and there is often knock-knee. The hairs of the body are scanty, and the genital organs remain infantile.

Myxœdema was first described by Gull as 'a cretinoid state supervening in adult life in women.' In it the

thyroid is always diseased, the acini being atrophied, and the connective tissue hypertrophied. The symptoms are due either to auto-intoxication, the result of the accumulation in the blood of substances normally destroyed by the thyroid, or to absence of the secretion. The latter view is the more probable.

The organism tends towards an anabolic rather than a katabolic condition; the vital fire glimmers rather than blazes (as in exophthalmic goitre), the output of carbonic acid and urea being diminished, while the weight increases.

The skin of the body becomes loose, flabby, and thickened. The alæ nasi, eyelids, and lips become swollen and puffy, as also the fingers and toes. These changes depend upon an increase in the connective and adipose tissues of the parts.

As Halliburton points out, the mucin is not necessarily in excess in the tissues, for in only two out of ten cases of myxœdema examined by him did he find an excess. Hence the name by which the disease is generally known is not well chosen.

Implantation of a sheep's thyroid into the subcutaneous tissues, or the administration of thyroid extract, may effect a striking improvement in the symptoms.

Cachexia Strumipriva is the condition which results from complete extirpation of the thyroid. The symptoms closely resemble those of myxœdema.

Suprarenal Capsules, or Adrenals.

Oliver and Schäfer obtained from the medullary portion of the suprarenal capsules a substance—*adrenalin*—which has a special action in contracting the peripheral arterioles, and causing a great rise in the arterial blood-pressure.

According to Abelous and Langlois, one of the functions of the suprarenals is to destroy the toxic products of muscular and mental exertion, for they found that if these organs are removed and the animal is made to perform muscular work, toxic symptoms soon develop.

Addison's Disease is characterized by great muscular weakness, low blood-pressure, rapid, feeble pulse, a tendency to syncope, vomiting, and pigmentation of the skin, which symptoms are always associated with disease of

the suprarenal capsules. In the great majority of cases, if not all, the change consists in a *tubercular destruction* of the gland tissue.

New growths sometimes occur, but they are rare, and it is very doubtful if they are ever the cause of genuine Addison's disease, inasmuch as they do not, like tubercle, destroy the suprarenals on both sides.

Accessory Adrenals are not uncommon. They are in the form of solid lumps, near the main glands, or in the capsule of the kidney. They have also been found in different parts of the abdominal cavity (liver, broad ligaments, spermatic cord, epididymis). Tumours may develop from these accessory adrenals, more especially when they are situated in the kidney.

The Pituitary Body.

This structure is peculiar in being developed in part from the alimentary canal, and in part from the brain. It consists of two lobes: an anterior, or glandular—a diverticulum from the pharynx—and a posterior, or nervous, developed from the embryonic mid-brain.

Acromegaly is a disease characterized by hypertrophy of the *bones* of the face, hands, and feet. In the face, the lower jaw especially is affected, projecting in advanced cases beyond the upper. The soft part of the nose, the lobe of the ear, the lips and tongue, the hands and feet, also become thickened, and the patient in many respects reverts to the simian type.

In all cases which have been examined after death the pituitary body has been found hypertrophied, or the seat of a tumour. Probably the disease results from an excess of, or some alteration in, the secretion of this gland. (*Giantism* is due to an enlargement of the pituitary body in the growing years of youth, and *acromegaly* to an enlargement when the normal period of growth has ceased.)

The acromegalous man takes on many of the features of the anthropoid ape, the former resembling the latter in the following among other particulars: In the possession of cranial crests, prominent supra-orbital ridges and malars, and massive jaws; in the prominence of the eyes, wrinkling of the lids, furrowing of the forehead, breadth and fleshiness of the nose, and thickness of the lips; in the shortness and thickness of the neck; in the backward convexity of the cervico-dorsal spine and consequent stoop; in the long sagittal diameter of the thorax and the abdominal character

of the breathing; in the bowing of the legs and massiveness of the skeletal and muscular systems; in the existence of pads, separated by deep furrows, on the palms and soles, and in the longitudinal striation of the nails; in the coarseness and looseness of the skin and tendency to pigmentation, and in the coarseness and excessive growth of hair; in the depth of the voice; in the activity of the cutaneous glands, and susceptibility to cold (H. Campbell).

The Thymus Gland.

This gland is developed from the pharynx, and when fully formed is chiefly composed of lymphoid tissue, the corpuscles of Hassal representing the original hypoblastic elements. The gland begins to atrophy by the time of puberty, and after the twentieth year should be only represented by a mass of fatty connective tissue spread out over the superior mediastinum and front of the pericardium.

The functions of the thymus are intimately connected with the growth of the child. Its complete removal in the animal arrests the development of the bones.

Hypertrophy of the Thymus.—The normal weight of the thymus is 5 drachms; if it exceeds this, the gland is hypertrophied. When this occurs, there is often a slight cyanosis of the face, which is liable to deepen when the patient becomes breathless. Attacks of suffocation may come on suddenly, often at night, and may cause sudden death, especially in children under two years.

Status Lymphaticus is the condition sometimes met with in children and young adults, characterized by persistent and enlarged thymus, hypertrophied lymphatic glands, and increase in the lymphoid tissue of the tonsils, base of the tongue, of Peyer's patches, and of the Malpighian bodies in the spleen. Fatty degeneration of the heart sometimes coexists. The condition has been found in a number of cases in which sudden death had occurred during the administration of anæsthetics, as well as in certain cases of death from trivial causes.

Other Hormonic Affections.

Premature Puberty.—Puberty may make its appearance as early as the second year, owing to the premature entrance into the blood of some hormone, or hormones (p. 18), which normally bring it about. In some of these cases there may be considerable muscular development

and a large deposit of fat, and in such the adrenals are generally involved in disease.

Infantilism.—In this condition development does not proceed beyond the infantile stage. It is probably due to the absence from the blood of some substance, or substances, necessary to normal development. One such substance appears to be provided by the pancreas, for cases in which diarrhœa has been a prominent symptom have been recorded (by Byrom Bramwell and others) which have been greatly improved by the administration of pancreatic extract.

Premature Senility.—This is due to the premature entrance into the blood of substances which promote senile changes in the tissues, or to the absence from the blood of substances which keep the tissues youthful.

Before the patient has reached the age of twenty, it may be, the skin becomes wrinkled, the hair blanched, the spine rigid, the arteries atheromatous, and the tissues generally exhibit other features characteristic of old age.

The degenerative changes occurring in what may be termed *normal senility* are not so much due to a wearing out of the tissues, as to the presence in the blood of substances which bring them about. Senile degeneration is, in fact, essentially a suicidal process.

SYPHILIS.

'Syphilis constitutes one-third of human pathology' (Gaucher).

According to the researches of Schaudinn and Hoffmann, syphilis is due to the presence of the *Treponema pallidum*, this organism having been found—

Acquired syphilis	in the primary sores.
	in the skin lesions.
	in the mucous membrane lesions.
	in the lymphatic glands.
	in the blood and lymph.
Congenital syphilis	in the skin lesions.
	in the liver.
	in the spleen.
	in the lymphatic glands.
	in the lungs.
	in the blood.

The organisms are found most abundantly in situations where infectivity is most intense—*e.g.*, mucous tubercles. The tissues of a syphilitic infant swarm with them, especially the liver, spleen, and lungs.

Metchnikoff and Roux have also discovered them in the syphilitic lesions of the higher apes inoculated with the virus taken from human beings, but they have not as yet been cultivated outside the body.

The organism is also found in the tertiary lesions, but very rarely, a circumstance probably due to its having undergone a change of form, which alters its staining properties. It has never been demonstrated in general paralysis of the insane or in tabes dorsalis.

The *Treponema pallidum* is supposed to be *a protozoon*, and, as described by Schaudinn, is a long threadlike organism, from 4 μ to 14 μ in length and 0·25 μ in breadth, tapering at both ends, with eight to sixteen corkscrew-like spirals, which are visible in the living animal, both while in movement and at rest, and which give it a 'twisted' appearance. It is actively motile, propelling itself by rotating around its longitudinal axis, first in one direction and then in another,

An organism found in yaws (*Spirochæta pertenuis*) closely resembles the *Treponema pallidum*.

'We may regard syphilis as a general micro-organismal invasion of the body from a point of inoculation of the lymph-stream, secondary invasion of the blood-stream, polyadenitis, and eruptions by emigration of the parasites from the blood-stream to the perivascular lymphatics of the skin, mucous membranes, viscera, and meninges' (Mott).

Primary Lesion.—The chancre, or 'hard sore,' occurs at the site of inoculation, being the local expression of the reaction of the tissues to the *Treponema pallidum*. It is generally in the form of a papule, with an indurated base. Slight ulceration of the surface takes place, and in about six weeks' time (under treatment) the entire chancre disappears by absorption, leaving little or no scarring. Inasmuch as it is painless, and yields but a slight discharge, it may pass unobserved by the patient. The chancre is composed of lymphoid cells, proliferated connective tissue, and endothelial cells, with occasional giant

cells. It is non-vascular. Should the sore become phagedænic, it indicates a mixed infection.

Secondary Lesions.—These are essentially epithelial (epiblastic and hypoblastic), being characterized by cutaneous eruptions, mucous tubercles, and shallow ulcers on the tongue, soft palate, and pillars of the fauces. They are probably due to the excretion of the specific toxin by the skin and mucous membranes.

Tertiary Lesions.—By the time this stage is reached, which may be as early as six months after the primary infection, the treponema has probably undergone some change in form, and produces a different toxin. This would account for the difference in the lesions as compared with those found in the secondary stage. Or it is possible that tertiary syphilis 'may be the result in some cases of secondary lesions which have remained latent until roused into activity by some exciting factor, such as exposure to cold, trauma, and toxæmia—microbial or otherwise' (Mott).

Sir Samuel Wilks has always maintained that 'the term tertiary syphilis is objectionable; there is no real distinction between the primary, secondary, and tertiary forms.'

Tertiary lesions affect *par excellence* the mesoblastic tissues, and the history of this stage of the disease is the history of a particular form of granulation tissue, the *syphiloma* or *gumma*, composed of lymphoid cells, connective-tissue cells, endothelial cells, and sometimes giant cells. Between the cells are new bloodvessels. This granulation tissue may occur in two forms: (i.) in concentration, when it is called the *gumma;* or as (ii.) *a diffused gummatous infiltration.*

(i.) A gumma is most liable to form on parts exposed to injury—*e.g.*, round about the knee and on the liver. It may resolve under treatment if begun early, or it may undergo necrosis from syphilitic endarteritis, and subsequent thrombosis of the supplying arteries. A gumma situated on an exposed surface is specially liable to ulcerate and to destroy the tissues deeply.

(ii.) A diffused gummatous infiltration may, like the gumma, resolve under treatment, or it may organize into connective tissue.

Any organ of the body may be affected with one or both

of these lesions; for example, there may be a diffused gummatous infiltration of the liver, or gummata on its surface, and this applies to all the viscera, to the nervous system, to the bones, and to the bloodvessels.

Syphilitic affections of the various organs are dealt with under their respective headings; those of the nervous system call for special notice.

Syphilis of the Nervous System.

The toxin of syphilis probably acts upon the nervous system in two ways—(*a*) Upon the nerve elements, causing their degeneration; and (*b*) upon the bloodvessels, membranes, and neuroglia, causing thickening of these structures.

Among the more important changes thus induced are the following :

Syphilitic Endarteritis, either in the form of nodular thickenings (gummata), or of a diffuse gummatous infiltration of the arteries of the brain, especially at the base (which, if complicated by thrombosis, may give rise to hemiplegia), and of the spinal cord.

'I have not seen a case of syphilis of the central nervous system post mortem in which the vessels have been perfectly healthy; usually they were extensively diseased' (Mott).

Gummatous Meningitis, especially at the base of the brain (involving the cranial nerves), and of the spinal cord.

Gummata, beginning in the meninges and spreading to the brain surface (often causing Jacksonian epilepsy).

General Paralysis of the Insane. — Syphilis is the essential cause of this disease. Eight general paralytics were inoculated with syphilis by Krafft-Ebing, and they all showed immunity from the disease. Mott has recorded many cases of general paralysis occurring in children afflicted with congenital syphilis.

The essential pathological changes occur in the cerebral cortex, and consist of :

Thickening and adherence of the meninges.

Thickening of the neuroglia.

Thickening of the walls of the arteries.

Atrophy of the neurons. (This is thought to be a primary change.)

On removing the membranes, the surface of the brain tears away with them ('decortization'), leaving a characteristic worm-eaten appearance, especially marked over the frontal and central convolutions.

Changes in the cord similar to those met with in tabes dorsalis are generally found. They would doubtless be still more frequent and pronounced if the disease did not run such a rapidly fatal course. There is always lymphocytosis of the cerebro-spinal fluid.

Tabes Dorsalis.—This also is a manifestation of syphilis. The morbid changes are, *mutatis mutandis*, the same as those found in general paralysis. The disease usually starts as what appears to be a *meningo-neuritis* of the posterior roots in the dorso-lumbar region of the cord, although the process is probably to a large extent a primary atrophy of the sensory nerve fibres constituting the posterior roots. The continuations of these fibres in the posterior columns of the cord atrophy. Other regions of the cord are also sometimes involved. In course of time the posterior roots undergo marked atrophy.

The Argyll-Robertson phenomenon (=pupils react to accommodation, but not to light) is thought to be due to a lesion of the ciliary ganglion within the orbit. (With very rare exceptions, it indicates syphilis of the nervous system.) Lymphocytosis of the cerebro-spinal fluid is always present.

In cases complicated by 'Charcot's joint disease' and 'perforating' ulcer of the foot, the nerves supplying the affected parts have been found degenerated.

The Wassermann reaction is found in about 90 per cent. of cases of general paralysis of the insane, and in about 75 per cent. of cases of tabes dorsalis.

CHRONIC ALCOHOLISM.

The morbid changes observed in chronic alcoholism are:

An increase of the fibrous at the expense of the higher elements of the tissues. This is particularly marked in the liver, arteries, and nervous system.

A tendency to fatty degeneration, especially of the heart. At the coroners' inquests held in London the

common cause of sudden death in drunkards is found to be fatty degeneration of the heart.

A tendency to inflammations, notably to catarrh of the mucous membranes, alimentary and bronchial. Alcoholic peripheral neuritis occurs chiefly in women.

The tendency of alcoholics to inflammations is largely due to their diminished resistance to pathogenetic bacteria. It is for this reason that the mortality from such diseases as pneumonia is so high among them.

The above-mentioned changes may be caused either by the direct action of the alcohol on the tissues, or by bacterial toxins developed in the catarrhal alimentary tract. Probably both factors co-operate.

'When the sot has descended through his chosen course of imbecility or dropsy to the dead-house, Morbid Anatomy is ready to receive him—knows him well. At the post-mortem she would say: "Liver hard and nodulated; brain dense and small, its coverings thick." And if you would listen to her unattractive but interesting tale, she would trace throughout the sot's body a series of changes which leave unaltered no part of him worth speaking of. She would tell you that the once delicate, filmy texture which, when he was young, had surrounded like a pure atmosphere every fibre and tube of his mechanism, making him lithe and supple, has now become rather a dense fog than a pure atmosphere—dense stuff which, instead of lubricating, has closed in upon and crushed out of existence more and more of the fibres and tubes, especially in the brain and liver—whence the imbecility and the dropsy' (Moxon).

'Alcohol acts particularly on the higher centres of the brain, and a drunken man may exhibit the abstract and brief chronicle of insanity, going through its successive phases in a short period of time' (Maudsley).

DISEASES OF BONE.

The structure of bone is that of a specialized connective tissue impregnated with lime-salts. The periosteum on the outside of a bone is continuous with the endosteum (marrow) of the inside, and numerous bloodvessels pass from the one to the other.

This vascular continuity explains how inflammation beginning primarily in either periosteum, bone, or endosteum, is liable sooner or later to involve all three.

General Principles.

Osteitis, or inflammation of bone, is generally the result of tubercle, syphilis, or other microbic infection.

First Stage: *Hyperæmia.*—The bloodvessels dilate, exudation of inflammatory lymph begins, and the bone assumes a pink colour.

Second Stage: *Rarefaction.*—Exudation of inflammatory lymph continues, the lime-salts are dissolved out, and the bone substance is partially absorbed, the compact tissue becoming rarefied and the cancellous still more cancellous. This rarefying process is effected in part by the action of phagocytes, in part by the peptonizing action of bacterial toxins, and possibly in part also by the solvent action of the inflammatory lymph under high pressure.

In the dry specimen the bone at this stage presents a 'worm-eaten' appearance.

Third Stage: *Caries*, *Abscess*, *Sclerosis.*—Should the rarefying process persist long enough, the whole of the affected bone dissolves away by a process of molecular death, or *caries*. If after this has occurred, the inflammatory exudate, consisting largely of pus, becomes imprisoned by the surrounding bone, the result is an *abscess*. If, on the other hand, the exudate poured out during the period of rarefaction organizes, *sclerosis* results—*i.e.*, the formation of hard, dense bone. The cancellous spaces are in this way obliterated and the medullary cavity is filled up, this being the usual condition of the terminal portion of bone in stumps after amputation.

Acute Infective Osteomyelitis (Pan-Osteitis).

This disease attacks the long bones, the larger more frequently than the smaller. It is always caused by the action of *staphylococci*, or *streptococci*, the organisms entering the body either through an external wound, or in consequence of some infecting focus in the mouth, throat, or other part. Lowered vitality is an important predisposing factor.

The disease is characterized by the rapid formation of

pus. It presents three types, according to the position of the initial lesion, which may be either—

1. In the periosteum,
2. In the interior of the shaft, or
3. In the epiphysis (acute epiphysitis).

If the disease begins beneath the periosteum and the pus is not let out by a timely incision, the fluid, spreading far and wide, leaves the bone bare and dead. In this way a portion, or, it may be, the whole shaft, of the bone perishes, the condition being known as *acute necrosis of bone*. This form is generally limited to the shaft, for the disease does not usually spread to the epiphysis, which is protected by the intermediate cartilage; the neighbouring joint also escapes as a rule.

If the disease begins in the interior of the shaft, necrosis is brought about by a strangulation of the bloodvessels combined with the toxic action of the bacterial products. This is the ordinary *acute infective osteomyelitis*. Should it remain untreated, *pyæmia* is very likely to occur, as the infective thrombi in the veins are liable to disintegrate and be discharged into the blood-stream as septic emboli.

If the disease begins in the epiphysis, it is generally localized to this part, and is known as *acute epiphysitis*.

Caries.

Caries is the molecular dissolution of a portion of bone, resulting from the continuation of the rarefying process of osteitis, being analogous to ulceration of the soft tissues. It may occur in any bone, but is commonly met with *in the cancellous tissue* of the epiphyses, the bodies of the vertebræ, the carpus, and the tarsus. By far the commonest cause is tubercle, and when thus originating it may be regarded as a *phthisis of bone*. When dead bone separates, it does so by caries taking place in the adjacent portions of the surrounding living bone.

Dry Caries.—The absorption of bone resulting from pressure—*e.g.*, of an aneurism—is sometimes spoken of as 'dry caries.' The process is of the nature of an atrophy.

Necrosis.

Necrosis is the death of bone in mass, and is analogous to gangrene of the soft parts. It commonly affects the *compact tissue* of the shafts of the long bones. In all cases the cause is a cutting off of the blood-supply, either by injury or inflammation (periostitis, osteitis, or osteomyelitis). Necrosed bone is bloodless, dry, and white in colour, but on exposure to the air it often becomes brown.

Separation of Dead Bone.—The surrounding bone becomes inflamed, caries results, and the loosened dead bone, now called a *sequestrum*, lies bathed in pus in a cavity bounded by granulation tissue, and lined with a 'pyogenic membrane.' The periosteum covering the sequestrum may form a new layer of bone over it—the *involucrum*. This is perforated by holes—*cloacæ*—to allow of the escape of pus.

Tuberculosis of Bone.

Tubercle may form in the periosteum, in the epiphyses, or in the diaphyses. Its favourite position is the *cancellous tissue* of the epiphyses, the bodies of the vertebræ, the carpus, and the tarsus—in other words, bone in the neighbourhood of a joint.

Syphilitic Diseases of Bone.

In the *secondary stage* of syphilis a fleeting periostitis may occur.

In the *tertiary stage* the bone affections which may occur are similar to those characterizing this stage of the disease elsewhere. Gummatous material may form in either the periosteum or the bone, and give rise to *caries*, *necrosis*, or *sclerosis*. Caries and necrosis may occur together (*cario-necrosis*); a gumma may be surrounded by hard, sclerosed bone. Gummata are most likely to form on parts exposed to injury, and hence they are most often met with on the subcutaneous surfaces of bones, leading to the formation of 'nodes.' Syphilitic caries is commonest in the skull. Syphilitic sclerosis may be

widely diffused throughout the whole shaft of a long bone, and it may also occur in the bones of the cranial vault.

In both acquired and congenital syphilis the fingers and toes may be affected with periosteal gummata, giving rise to the condition known as *syphilitic dactylitis.*

In *congenital syphilis* the diseases of bone, according to Parrot, assume two principal forms :

1. Atrophic { Gelatiniform. / Osteochondritis.
2. Hypertrophic, or Osteophytic { Osteoid. / Fibro-spongoid.

1. In *gelatiniform atrophy* the bone tissue is replaced by a gelatinous substance.

In *osteochondritis* (sometimes called syphilitic epiphysitis) the cartilage between the epiphysis and the diaphysis becomes abnormally thick and loses its regular outline ; ossification stops short at calcification, the zone of calcified material being dense and brittle. As a result, fracture is liable to occur, and as the symptoms may resemble paralysis, Parrot has named this condition *syphilitic pseudo-paralysis.*

2. In the hypertrophic variety the new bone of the growing child may be hard and ivory-like, when it is termed *osteoid ;* or it may be fibroid in structure and very vascular, when it is termed *fibro-spongioid.* The two conditions may be combined : thus, the osteoid and spongioid material may be arranged in alternating layers. The most common sites for these changes are the ends of the humerus, femur, and tibia.

In the skull ' bosses ' of new bone may form around the fontanelles (' Parrot's nodes '), and these may become bridged over, and so give rise to the rounded, prominent forehead observed in later life in the subjects of this disease. In the occipital and parietal bones circumscribed areas of extremely thin bone, or even of membrane only, are sometimes met with. To this condition the name of *craniotabes* has been given. (In the Museum of the Royal College of Surgeons, London, are specimens presented by M. Parrot showing all these changes.)

Tumours of Bone.

The most common primary tumours of bone are the enchondromata, the osteomata, and the sarcomata. Secondary tumours may be either sarcomatous or carcinomatous.

Sarcomata of Bone.—In descending order of malignancy these tumours stand thus :

1. Periosteal sarcoma.
2. Endosteal sarcoma of diaphysis.
3. Endosteal sarcoma of epiphysis.

Periosteal sarcoma is of extreme malignancy. The third named is usually the ' myeloid ' variety, the favourite sites of which are the lower ends of the femur and radius, the upper ends of the tibia and humerus, and the lower jaw. This variety never causes secondary growths.

Rickets.

Rickets, first described by Glisson in 1650, is a blood disease, probably toxic in nature, affecting the nutrition of the entire organism, but as its most obtrusive pathological effects are registered in the bones, it comes in for consideration here. Sir William Jenner said it would be as reasonable to regard rickets as a disease of the bones only, as it would be to regard typhoid fever as merely a disease of Peyer's patches. The condition commonly attracts attention at about the sixth month after birth. There is probably no such thing as congenital rickets. The constitutional symptoms strongly suggest a *toxæmia:* the child is anæmic ; it is very irritable, and cries when handled, on account of a diffuse tenderness of the body ; it is restless during sleep, sweats freely about the head, and a slight degree of fever is often present ; the child, besides being irritable, is nervous and liable to convulsions, such as might be due to a convulsant poison. There is also a tendency to inflammation of the mucous membranes, notably of those lining the alimentary and respiratory tracts.

The essential cause is probably *a toxin generated in the*

alimentary canal as the result of improper feeding. A child who is simply starved does not get rickets. This suggests that the disease is due not to the absence of an essential element in the blood, but rather to the presence in it of some noxious substance (or substances). The toxin, being absorbed into the system, perverts nutrition, particularly in places where developmental activity is great—*e.g.*, in the growing parts of bones where there are definite signs of irritation.

The most characteristic changes occur at the epiphyses and beneath the periosteum of the long bones. Thus the cushion of cartilage between the epiphysis and the diaphysis is thicker than normal, and the plane of ossification on the diaphyseal side of the cartilage, instead of being even, is irregular. The cartilage cells divide with excessive rapidity, suggesting the action of an irritant. The newly-formed bone is unduly soft, chemical examination showing it to be very deficient in lime-salts.

Similar changes take place beneath the periosteum, the new bone laid down by this membrane being softer and more spongy than in health, and as a consequence the bones bend, giving rise to various characteristic deformities. These are more marked in some bones than in others, although the entire osseous system is affected.

The anterior fontanelle remains open longer than the normal eighteen months after birth, and the teeth erupt late. From pressure by the pillow, soft, decalcified areas are liable to form in the occipital and parietal bones (=craniotabes), though this condition generally (some say always) indicates congenital syphilis.

If the child lies much on its back, the occipital bone is liable to become flattened and the frontal bone to become prominent; for the bones of the cranium are easily displaced, on account of the late closure of the fontanelles and the yielding nature of the sutures. The cranial vertex is often flat, and the coronal suture may be 'keeled.'

In the spine there is usually some kyphosis, and the child may not begin to sit up until after the first year, instead of, as normally happens, at about the seventh month. The sternum is thrown forward ('pigeon-breast'), and there is considerable thickening of the ribs at their junction with the cartilages ('beaded' ribs). It should,

however, be remembered that a small degree of beading is normal.

Rickets is the commonest cause of deformed pelvis. The sacral promontory projects forwards from the downward pressure of the weight of the body, and the brim is 'kidney-shaped.' Sometimes the symphysis pubis is pulled backwards by the abdominal recti, giving rise to the 'hour-glass' pelvis.

The most notable changes in the long bones are enlargement at the junction of the shaft with the epiphysis, from swelling of the epiphyseal cartilage, exaggeration of the normal curvatures, and the development of curves due to the traction of powerful muscles—*e.g.*, an outward curve of the humerus, corresponding to the insertion of the deltoid. The bones of the forearm are bent outwards in their lower thirds. The femur shows a long forward curve. The bones of the leg are bent outwards and forwards in their lower thirds. Strong bony buttresses usually develop in the concavities of the curvatures, where the new rickety bone is laid down most abundantly.

The tendency of the disease is towards spontaneous cure, *the bones in course of time becoming normally ossified in their deformed positions.*

Infantile Scurvy (Scurvy Rickets).

In this disease hæmorrhagic effusions take place beneath the periosteum of the long bones, more particularly of the femur and tibia. Hæmorrhages may also occur in the interior of the long bones and ribs. Separation of the epiphyses is not uncommon. Spongy gums, and hæmorrhages from mucous membranes, and into the skin and the joints, are usually also found.

Achondroplasia.

This disease is due to imperfect ossification of the *epiphyseal cartilages.* It is sometimes inaccurately called fœtal rickets, differing from ordinary rickets in that it is always *congenital.* The bones which develop from cartilage are alone affected.

The development *in length* of the diaphyses of the long

bones is defective, though they are normal in thickness: hence the limbs are short and stunted. There is no bending, and there are no abnormal curves. The bones at the base of the skull ankylose early, and as those at the vault grow naturally, the head looks unusually big. The bridge of the nose is depressed. The bones which develop from membrane being unaffected, the clavicles, ribs, sternum, and vertebral column are all of normal size. Death occurs in most cases a few days after birth. Those who survive grow up dwarfs.

Osteomalacia (Mollities Ossium).

This disease is essentially one of *decalcification*, the lime-salts being absorbed and the bones in consequence becoming soft, bent, and liable to spontaneous fractures which do not unite. The disease is almost entirely confined to women, and generally develops during pregnancy. The bones usually affected are those of the *pelvis*, the *vertebral column*, and the *ribs*.

The morbid change begins in the interior of the bones, the medulla being replaced by a tissue resembling the splenic pulp. The decalcification proceeds from within outwards, until all that is left of the original bone is a thin layer of compact tissue beneath the periosteum. As in a few cases the removal of diseased ovaries has resulted in arrest of the disease, it has been suggested that the solution of the bone-salts which takes place in it may be due to the action of an abnormal ovarian secretion.

Osteitis Deformans.

This disease was first described by Sir James Paget. 'The disease affects most frequently the long bones of the lower extremities and the skull, and is usually symmetrical. The bones enlarge and soften, and those bearing weight yield and become unnaturally curved. The spine may sink and seem to shorten, with greatly increased dorsal and lumbar curves; the pelvis may become wide; the necks of the femora may become nearly horizontal, but the limbs, however misshapen, remain strong and fit to support the trunk' (Paget).

The calvarium may become enormously thickened, the patient noticing that he has to use larger and larger hats, while his stature becomes less and less. The disease begins after middle life, and its progress is very slow, sometimes lasting as many as twenty years. The enlargement and softening of the bones are due to the development of soft, spongy, and highly vascular new bone.

Acromegaly.

This disease is characterized by excessive growth of the bones (as well as the soft tissues) of the hands, feet, face, and other parts. The lower jaw is increased in size and projects forwards ; the supra-orbital ridges are prominent (see p. 173).

Leontiasis Ossea.

In this disease the bones of the face and cranium become greatly thickened.

Hypertrophic Pulmonary Osteo-Arthropathy.

This disease is characterized by enlargement of the *terminal phalanges* of the fingers and toes and neighbouring bones, with incurvation of the nails. It is associated with bronchiectasis, empyema, and pulmonary tuberculosis, and is probably caused partly by absorption of toxic material from the diseased lung or pleura, and partly by the sluggishness of the circulation resulting from the pulmonary obstruction.

DISEASES OF THE JOINTS.

Tuberculosis of the Joints.

Tuberculosis of a joint may be compared with tuberculosis of the lung. The disease may begin in the synovial membrane, which is the morphological equivalent of the pleura (tubercular synovitis), or may begin in the head of the bone, which is the morphological equivalent of the lung (tubercular osteitis). It never begins in the arthritic cartilage.

Tubercular synovitis affects, as a rule, the hinge-joints —viz., the elbow, wrist, knee, and ankle. Tubercles form in the synovial membrane, causing it to become thickened, gelatinous, and pulpy. The synovial fringes spread over the articular surfaces, covering them like a veil, and from the under surface of this veil small processes penetrate into the underlying cartilage, a condition compared by Billroth to ivy creeping over a wall and becoming gradually attached by its roots. The cartilage now becomes ulcerated, and finally, unless the tubercular process is arrested, the underlying bone is invaded and becomes carious.

Owing to caseation and suppuration of the tubercular material, the entire synovial membrane is converted into a pyogenic membrane similar to that found in a chronic tubercular abscess, the pus eventually burrowing to the exterior. The whole interior of the joint in this way becomes disorganized.

Tubercular osteitis affects the ball-and-socket joints, and is well illustrated in the case of tubercular disease of the hip-joint. The process here usually starts in the epiphysis of the femur, either close to the intermediary cartilage or just beneath the articular cartilage of the head. Caries supervenes, and the inflammatory products escape into the cavity of the joint. The synovial membrane and ligaments become secondarily affected, and the whole joint tends to disorganization, the acetabulum being inoculated by contact with the carious head of the femur, and may even become perforated. In some cases the epiphysis gets detached and lies loose in the joint. The pus generally escapes through the thinnest part of the capsule—*i.e.*, at its posterior part. It then burrows forwards beneath the gluteus minimus, the medius, and the tensor vaginæ femoris, and ultimately forms a swelling beneath the anterior superior iliac spine.

Complications of Tubercular Arthritis.—If an abscess bursts and becomes septic, *amyloid disease* is likely to develop. At any time during the progress of tubercular arthritis *acute miliary tuberculosis* (either of the pia mater, lungs, or abdominal viscera) may be set up.

Complete disorganization does not of necessity follow in all cases of tubercular joint disease. In favourable

cases, especially if treatment has been begun early, the disease may be arrested, the inflammatory products being in part absorbed, and in part converted into fibrous tissue.

In rare cases tubercular arthritis starts from a *tuberculous periostitis*, or from a *tuberculous bursa*.

Arthritis Deformans.

This term embraces several types distinct alike in their ætiology, pathological features, and clinical course. The cause, in certain of them at least, is *probably a toxin*, acting either directly on the joint structures, or on the nerves supplying these parts. The disease presents two main types (though numerous intermediary forms are met with): *Osteo-Arthritis*, in which the changes first appear in the articular cartilages and bones; and *Rheumatoid Arthritis*, in which the synovial periarticular structures are most affected.

Osteo-Arthritis generally comes on after middle life. The morbid changes are characteristically displayed in *morbus coxæ senilis*. These changes involve—

The articular cartilages.
The underlying bones.
The synovial membrane.
The interarticular ligaments.
The surrounding muscles.

The hyaline matrix of the *articular cartilage* becomes fibrillated, and the cartilage cells proliferate and escape into the joint. The surface of the cartilage now loses its polish, assuming a velvety appearance, and in course of time its central part is worn down, and the underlying bone, highly polished like porcelain or ivory, is exposed.

While these changes are in progress, the circumference of the cartilage becomes irregularly thickened ('lipping'), sometimes developing flange-like outgrowths, or *ecchondroses*, which have been likened to the gutterings of a wax candle. These ecchondroses may in course of time become ossified, when they are known as *osteophytes*.

The *synovial membrane* thickens, its fringes hypertrophy, and finally the whole membrane may assume a shaggy appearance. Occasionally nodules of cartilage

develop in the fringes, and these sometimes break off, forming 'loose bodies' in the joint.

The *interarticular ligaments* in course of time degenerate and wear away. In this way the ligamentum teres disappears from the hip-joint, the intracapsular part of the long tendon of the biceps from the shoulder-joint, and the crucial ligaments and interarticular cartilages disappear from the knee-joint.

The *muscles around the joint* tend to atrophy, a change often well marked when the disease attacks the shoulder, hip, or knee.

The above changes are all typically seen in *morbus coxæ senilis*, but they are also observed in that chronic symmetrical polyarticular affection (involving, it may be, all the joints in the body) for which Garrod would reserve the term *arthritis deformans*.

The enlargements of the end joints of the fingers met with in this disease are known as Heberden's nodes.

Rheumatoid Arthritis.—The affection just described must, clinically at least, be distinguished from another polyarticular affection to which Garrod would limit the term 'rheumatoid arthritis,' because the joint affection in it is more genuinely rheumatoid in character. The disease generally comes on in early adult life, involving many joints symmetrically. All the joints of the body may be affected. (N.B.—In gout and rheumatic fever the temporo-maxillary joints and cervical spine are practically never attacked.) Those of the fingers are apt to be involved early, causing these latter to be fusiform from swelling of the interphalangeal joints; hence the disease is sometimes known as the *fusiform* variety of rheumatoid arthritis. The joint affection is peri- rather than en-arthritic, though enarthritic changes, somewhat similar to those observed in arthritis deformans, may in course of time occur, for which reason some hold that the two diseases are fundamentally the same. The muscles about the affected joints undergo marked atrophy, and the contractions of the wasted muscles may cause considerable crippling.

A feature of this malady is its constitutional nature. It is manifestly a blood disease. The patient is anæmic his vitality is low, and he is apt to be febrile.

Still's Disease is allied to the last, if it is not actually the same disease, but, in addition to the joint affection, enlargement of the spleen and of the lymphatic glands is apt to occur. It is met with in children.

Neuropathic Arthritis.

This group of joint diseases is found in connection with certain diseases of the spinal cord and nerves, the most notable lesions being: tabes dorsalis, syringomyelia, spina bifida, hemiplegia, paraplegia, peripheral neuritis, and division of peripheral nerves.

Charcot's Joint Disease develops in connection with *tabes dorsalis*, generally during the pre-ataxic stage. The usual joints to be affected are those of the knee, hip, and shoulder. The onset is generally sudden; there is considerable swelling of the joint, but neither pain nor fever is present. A patient may go to bed well, and wake up in the morning with the joint distended, without any apparent cause.

This swelling is due in part to effusion into the joint, and in part to œdema of the soft tissues outside it (the 'œdema without pitting' of Charcot).

Although in a few cases the effusion may be absorbed (the 'benign' form of Charcot), the articulation returning to its normal state, it generally proceeds to rapid and complete non-inflammatory destruction of the articulation (the 'malign' form of Charcot), and culminates in the production of a 'flail joint,' movable in all directions, or in dislocation.

It is essentially a trophic lesion, the nerves going to the joint being found diseased.

The morbid changes characterizing it are: effusion into the joint, early disappearance of the ligaments and cartilages, and *great atrophy of the articular ends of the bones*. *Osteophytes* may form, sometimes in large numbers.

In Charcot's disease of the knee it is not uncommon to find *bursal swellings*, especially of the bursa which so frequently communicates with the joint—viz., that under the semimembranosus tendon.

Syringomyelia may be associated with a form of joint

disease similar to that occurring in tabes dorsalis, but the seat is *usually in the upper limb*. In this disease trophic lesions may be also found in the skin, such as *whitlows*, *ulcers*, and *gangrene* of the fingers. The pathology is the same as that observed in Charcot's joint disease. A similar condition of the soft parts occurs endemically under the name of 'Morvan's disease.'

Sometimes the joint affection in syringomyelia is similar to that characteristic of arthritis deformans.

Gonorrhœal Rheumatism.

This disease, sometimes called *young man's rheumatism*, is caused by the entrance into a joint either of the gonococcus, the gonococcus toxin, or the organisms or toxins of a mixed infection. One or several joints may be affected, as also sometimes fasciæ, tendon sheaths, bursæ, and the fibrous sheaths of nerves. The knee is most often attacked, the elbow, ankle, and wrist being other frequent sites. A very troublesome form is that which affects the ankle, the tarsal joints, and the fibrous structures in the sole, causing a severe form of flat-foot. In some cases there is iritis. The disease seldom sets in until the third or fourth week after contagion. It may be either *acute*, *subacute*, or *chronic*.

In the *acute* form there may be suppuration, and even complete disorganization of the joint. Sometimes it simulates rheumatic fever. The more common *subacute*, or *chronic*, form is characterized by a plastic exudation involving the ligaments and *periarticular structures*, and manifesting a marked tendency to the formation of new fibrous tissue, which leaves the joint permanently stiff. In those cases in which the larger joints are affected the patient may become quite crippled.

DEFORMITIES.

Branchial Fistula, Cleft-Palate, and Hare-Lip.

In order to understand the nature of these deformities it is necessary to recall some points in the normal development of the upper jaw and neighbouring parts. In early

fœtal life the anterior portion of the alimentary tube communicates with the exterior on either side by a number of slit-like openings—the *branchial clefts*, between which are the *branchial arches*. The first branchial cleft persists as the external auditory meatus, the tympanum, and the Eustachian tube. All the others should close. In some rare cases, however, the third or fourth remains partially unclosed, the result being a fistula (*branchial fistula*) opening on the surface of the body near the sternal head of the sterno-mastoid muscle. Similar fistulæ have also been met with below the glottis.

As development proceeds, the *first branchial arch* on either side *divides*, forming the two superior and the two

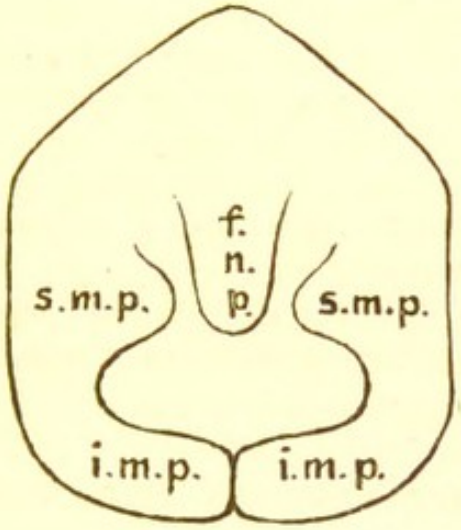

FIG. 16.

inferior maxillary processes. The two inferior processes unite in the middle line to form the lower jaw and the lower lip.

The two superior processes grow forwards to form the superior maxillæ, with the hard and the soft palate, the cheeks, and the lateral parts of the upper lip. They do not, however, unite anteriorly, but between them there grows downwards from the front of the skull the *naso-frontal process*, from which are developed the nose, the vomer, the nasal septum, and the premaxillæ carrying the incisor teeth and the central portion of the upper lip.

These various parts should unite by the ninth week

of fœtal life; should union be defective, the following deformities may occur:

Bifid uvula.
Fissure of the soft palate, with bifid uvula.
Fissure of both the soft and the hard palate.
Fissure of the hard palate only (very rare).
Fissure of the hard and the soft palates, combined with fissure of the alveolus and the lip on one side.
The same as the preceding paragraph, with fissure of the alveolus and lip *on both sides*.
Simple hare-lip.
Double hare-lip.

In the rare case of cleft of the hard palate the nasal septum is usually attached to one side of the palate, shutting off the nose from the mouth on that side. In only very rare cases is the lower border of the nasal septum free, so that *both* nasal cavities communicate with the mouth.

In double hare-lip the premaxilla and the central portion of the upper lip may be carried forwards as an appendage of the nose.

Very rarely the fissure of the hare-lip extends upwards on one side of the nose towards the inner side of the orbit (*patent orbital groove*).

Meningocele and Encephalocele.

A *meningocele* is a protrusion of the *dura mater* and the *arachnoid* through a congenital aperture in the skull, where it forms a soft fluctuating swelling, which contains cerebro-spinal fluid, and which increases in size on expiration, coughing, or crying. The most common site is the occipital bone, just above the foramen magnum, but it may also occur in the anterior fontanelle, at the root of the nose, at the base of the skull (protruding into the nasal passages or pharynx), and at the external angle of the orbit. It is often associated with hydrocephalus.

An *encephalocele* is a meningocele containing brain substance. It pulsates with the heart-beat.

A *hydrencephalocele* is an encephalocele enclosing a cavity filled with fluid continuous with that in the ventricles.

Spina Bifida.

Spina bifida is a congenital defect of the posterior part of the spinal canal, due to arrested development of the laminæ of one or more vertebræ, and generally accompanied by protrusion of the meninges and cord through the gap, in the form of a cystic tumour varying in size from a walnut to an orange. The usual position is the *lumbo-sacral region*, the laminæ of this part being the last to close in fœtal life. It is sometimes associated with hydrocephalus and talipes.

Varieties.—Meningocele, meningo-myelocele, syringo-myelocele, myelocele.

A *meningocele* consists of a protrusion of the dura mater and the arachnoid through the gap in the spinal canal; it contains cerebro-spinal fluid.

A *meningo-myelocele* is the most common form of spina bifida. It consists of a meningocele plus a portion of the spinal cord and nerves.

A *syringo-myelocele* is rare. It is similar to the last, but the central canal of the spinal cord is distended, the posterior part of the cord being spread out over the interior of the sac.

A *myelocele* is the condition resulting from non-closure of the primitive medullary groove, the central canal opening on the surface.

Torticollis.

Torticollis is a deformity caused by contraction of one of the sterno-mastoid muscles (often of other muscles also), by which the head is drawn downwards towards, and rotated away from, the affected side.

The deformity may be congenital, or it may appear soon after birth. In the former case it is due to an arrest of development, and in the latter to partial rupture of the sterno-mastoid during the third stage of labour. In childhood it may come on after measles and scarlatina, usually as the result of inflamed cervical glands. In some cases it arises from irritation of the spinal accessory nerve. Occasionally it is *spasmodic*, disappearing when the patient is anæsthetized.

If torticollis lasts for any length of time, the sterno-

mastoid, the deep cervical muscles, and the anterior portion of the trapezius become shortened, and the cervical vertebræ rotated, and lateral curvature of the spine may set in.

The congenital variety, unless surgically treated, tends to produce asymmetrical growth of the head.

Lateral Curvature of the Spine (Scoliosis).

This deformity commonly results from *weakness of the spinal muscles*, and commences in almost all such cases at about the period of puberty. It may also be due to the shortening of a limb, or the falling in of the ribs after an empyema.

There is a *primary curve*, generally in the dorsal region and convex to the right, with *secondary* or compensatory curves above and below, in a direction opposite to that of the primary curve, and with the object of maintaining the body in the upright position. In addition to the lateral curvature, *the vertebræ are rotated on their vertical axes*, the front of their bodies moving towards the convexity of the curve, and the spines towards the concavity. In this way the ribs on the convex side, together with the shoulder ('growing-out shoulder'), are thrown backwards and widely separated, while on the concave side they are thrown forwards and crowded together.

If the condition remains untreated, the intervertebral discs become permanently wedge-shaped, the base of the wedge being directed towards the convexity of the curve. In old-standing and advanced cases the bodies of the vertebræ also become wedge-shaped.

Lateral curvature is common in Friedreich's disease, and in syringomyelia. It also occurs secondary to pulmonary collapse—*e.g.*, after pleural effusion.

Angular Curvature of the Spine.

This deformity, also called Pott's curvature, is caused by the destruction of one or more of the bodies of the vertebræ by *tubercular caries* before adult life is reached. The disease may occur in any part of the spine, but its usual starting-point is the *dorso-lumbar region*, the caries

beginning either beneath the periosteum on the anterior surface of the vertebral bodies, or in the cancellous tissue of their interior. The affected bodies and adjacent intervertebral discs being destroyed, a gap is left, and in the case of the growing individual the upper part of the spinal column then falls forward upon the lower to form an angle—the so-called 'angular curvature' of the spine—while the lower portion moves backwards in compensation. Tubercular disease of the spine rarely causes angular curvature in the adult.

If repair takes place, the gap is filled in by a buttress of new bone or by fibrous tissue, and at the same time the laminæ and spines of the neural arches usually become ankylosed, and so act as a kind of splint.

Spinal abscess is the usual accompaniment of caries of the vertebræ. As the pus accumulates it travels along the lines of least resistance, either following the course of a bloodvessel or burrowing beneath fasciæ. When the disease is seated in the cervical region, the pus may point in the pharynx (*post-pharyngeal abscess*), or pass along the back of the œsophagus into the posterior mediastinum, or it may work its way into the posterior triangle of the neck, and even sometimes extend into the axilla.

When the disease is seated in the upper or the mid-dorsal region, the pus usually passes backwards along the posterior branches of the intercostal arteries, and forms a swelling close to the spinous processes (*dorsal abscess*). When the disease is seated in the lower dorsal, or lumbar region, the pus may pass backwards and form a swelling just external to the erector spinæ muscle (*lumbar abscess*).

As a rule, however, when the disease attacks the dorso-lumbar region, the pus burrows into the psoas muscle and forms a

Psoas abscess, the course of which is determined by the attachments of the ilio-psoas fascia.

The ilio-psoas fascia, which invests both the psoas and the iliacus muscles, is attached above to the ligamentum arcuatum internum, below to the iliac crest and brim of the true pelvis, internally to the front of the bodies of the lumbar vertebræ, externally to the transverse processes of the same vertebræ, and it ultimately follows the ilio-psoas tendon to its insertion into the small trochanter of the femur.

The abscess destroys the psoas muscle, extends downwards into the false pelvis over the iliacus muscle, and forms a large fluctuating swelling in the iliac fossa. Travelling still farther, the pus passes by a narrow neck beneath Poupart's ligament, just external to the femoral vessels, and then works its way behind the femoral vessels towards the insertion of the ilio-psoas tendon into the small trochanter of the femur, pointing at or close to the saphenous opening.

A typical psoas abscess, then, when fully developed, consists of four parts: a narrow track in the psoas muscle, an expanded portion over the iliac fossa, a narrow neck beneath Poupart's ligament, and a second expanded portion in the upper part of the thigh. Occasionally the psoas abscess is double.

In some cases the pus tracks down the thigh, and it has been known to travel as low down as the popliteal space, and even as far as the side of the tendo Achillis.

Occasionally the pus may enter the true pelvis, pass through the great sacro-sciatic notch, and form a gluteal abscess, or it may work its way along the side of the rectum and point in the ischio-rectal fossa.

Paraplegia occurs in but a small percentage of cases of angular curvature, the spinal cord generally escaping compression because the bending of the vertebral column takes place slowly; also because the spinal canal is considerably larger than the cord, which, moreover, is protected by the dura mater. When paraplegia does occur, the cause is pachymeningitis, or the pressure of inflammatory products, and not of the vertebræ. These products tend to become absorbed in process of time; hence the paraplegia is rarely permanent.

Coxa Vara.—The normal angle of elevation of the neck of the femur varies between 120 and 140 degrees. Coxa vara is that condition in which the angle is less than 120 degrees. In marked cases the head of the bone lies below the level of the great trochanter. It is now clearly established that the deformity is due to separation of the upper epiphysis of the femur, partial or complete, and the subsequent reunion in a faulty position.

Coxa Valga is the antithesis of coxa vara, the angle of elevation being over 140 degrees. It may result either

from separation of the upper epiphysis and its subsequent reunion in a faulty position or from rickets.

Genu Valgum, or '**Knock-Knee**,' is a deformity in which the tibia is deflected outwards from the femur, so that the external angle at the junction of the leg with the thigh is smaller than normal.

The deformity is *always acquired*, and usually double.

Knock-knee develops at two periods of life—

During early childhood.
During adolescence.

During Early Childhood.—The cause here is *rickets*. The lower end of the diaphysis of the femur and the upper end of the diaphysis of the tibia, being soft, bend. The result is an *apparent* lengthening of the internal condyle of the femur.

During Adolescence.—The strength of the knee-joint, like that of the arch of the foot, depends not only upon the ligaments, but also on the bracing action of the surrounding muscles. Normally, the weight of the body is transmitted more through the outer than through the inner condyle of the femur; if the muscles are weak, the weight is thrown still more upon the outer condyle, the growth of which is retarded, while that of the inner is accentuated. This increases the downward and inward obliquity of the femur.

In whichever way the deformity of knock-knee is produced, stretching of the internal lateral ligament occurs, while the external lateral ligament, the ilio-tibial band of the fascia lata, and the biceps undergo shortening. The patella is thrown outwards.

Genu Varum.—This deformity is the antithesis of genu valgum. It is practically always bilateral, and is due to rickets.

Talipes.

Deformities of the foot may be congenital or acquired, and they may occur in both extremities or in one only. The following are the different varieties :

Talipes Equinus, in which the heel is drawn up so that the patient walks on his toes, which are at a right

angle to the foot. This condition is rarely congenital, and is due to infantile paralysis of the dorsi-flexors of the foot, causing a secondary shortening of the muscles at the back of the leg. It has been known to result from an abscess in the calf.

Talipes Calcaneus, in which the anterior part of the foot is drawn up, forcing the patient to walk on the heel. It may be congenital, or the result of infantile paralysis of the muscles of the calf. It is rare.

Talipes Varus, in which the anterior part of the foot is twisted inwards at the calcaneo-cuboid and astragalo-scaphoid articulations, the patient walking on the outer border. It is generally associated with talipes equinus, pure talipes varus being of extreme rarity, and, when found, usually congenital.

Talipes Valgus, in which the anterior part of the foot is twisted outwards at the calcaneo-cuboid and astragalo-scaphoid articulations, the plantar arches being obliterated and the sole flattened. It may be either congenital or acquired, and when the latter is generally the result of infantile paralysis.

Talipes Equino-Varus is much the most frequent variety of talipes. The heel is drawn up and the foot twisted inwards, the patient walking on its outer border, where a bursa tends to form. The twisting takes place at the calcaneo-cuboid and astragalo-scaphoid articulations. In ordinary cases there is an increase in the obliquity of the neck of the astragalus.

Secondary contraction of the muscles, ligaments, and fasciæ takes place on the concave side of the foot. The tendo Achillis, and the tendons of both the tibialis anticus and the tibialis posticus, are shortened.

With the exception of the altered obliquity of the neck of the astragalus just mentioned, the tarsal bones are at first quite normal. In old-standing cases, however, those on the inner side of the foot, being compressed, remain undeveloped.

The most frequent cause is infantile paralysis. It may also be congenital when it affects both feet. The most probable explanation of this latter form of talipes is that, owing to some malposition of the fœtus *in utero*, or to deficiency of liquor amnii, or the presence of adventitious

bands, there is *an arrest of the unfolding process of the feet.*

'If the inversion of the foot, which is normal during the early periods of fœtal life, be maintained beyond the normal period of time, the muscles and ligaments will as a consequence be adaptively short on one aspect of the limb, and too long on the other; a normal position of inversion will finally become a deformity' (Parker and Shattock).

Talipes Calcaneo-Valgus, in which there is a combination of talipes calcaneus with talipes valgus. It is a very rare deformity.

Talipes Cavus, in which the main arch of the foot is abnormally developed. It is always an acquired condition, and is due to paralysis of the interossei muscles, with tonic contraction of the opposing muscles, in consequence of which the proximal phalanges become hyperextended upon the metatarsal bones, and the two distal ones flexed towards the sole.

The deformity is almost always combined with either talipes equinus or talipes equino-varus.

Flat-Foot, or Talipes Planus.—The plantar arches do not exist in the infant, but are acquired by exercise of the deep muscles of the calf (flexor longus digitorum, tibialis posticus, and flexor longus hallucis), and that of the tibialis anticus and the peroneus longus. The ligaments (more particularly the inferior calcaneo-scaphoid and the long and short plantar ligaments) simply help to keep the bones in position when the arch is finally established.

The primary cause of flat-foot would appear to be *muscular weakness;* this throws an extra strain upon the ligaments, which, lengthening, allow the instep gradually to sink, so that the sole becomes quite flat, and displays a tendency to eversion. The head of the astragalus, which forms the keystone to the main plantar arch, is displaced downwards, and in bad cases may rest upon the ground, the internal malleolus being perceptibly lowered. The inner side of the foot becomes lengthened.

The deformity generally comes on in early adult life, when the body-weight increases out of proportion to muscular development, and it is especially liable to occur if the patient has to carry a heavy weight, as, for instance, in the girl who has to carry an infant.

Hallux Valgus consists of an outward displacement of the great toe, so as to form a sharp angle with its metatarsal bone. It results from wearing faultily-shaped boots. As a consequence, the toes are crowded together and the distal end of the first metatarsal bone becomes prominent, being usually covered by a bursa (*bunion*).

Hammer-Toe is the deformity in which there is hyperextension of the proximal phalanx, with flexion of the second and extension of the third. Corns or bursæ usually form over the points of pressure. The deformity generally involves the second toe.

Although sometimes congenital, it is usually acquired as the result of the toes being crowded together from wearing pointed boots or high heels.

Dupuytren's Contraction is a shortening and thickening of the digital processes of the palmar fascia inserted into the middle phalanges. It commonly begins in the little finger, thence extending to the ring and middle fingers, all which are drawn down into the palm.

The cause is generally some long-continued pressure on the palm of the hand, such as may result from the use of certain tools, from playing golf, rowing, or from leaning on a walking-stick. In some cases contraction occurs without any apparent exciting cause, and it is then ascribed to gout or rheumatism.

On examining the hand, projecting ridges can be felt extending from the palm to the fingers, and if an attempt is made to strengthen the fingers, these ridges become taut. The skin over them is at first free, but subsequently becomes adherent.

The deformity can be readily diagnosed from contraction of the flexor tendons by the fact that the tendons above the wrist do not become tense when an attempt is made to straighten the fingers.

Adenoid Disease.

Adenoid disease ('adenoids') consists of a hypertrophy of the adenoid tissue in the naso-pharynx. The growth may entirely fill this cavity, causing a blockage of the Eustachian tubes and of the posterior nares, thus compelling the patient to breathe through the mouth.

The disease, though in rare instances congenital, does not generally begin until after the first year of life. It seldom begins after puberty, and if already existing at puberty, tends spontaneously to get well after this period.

Should the nasal passages be chronically blocked before the upper jaw (maxilla) has finished growing, this latter fails to develop properly, and there results what may be termed 'the mouth-breather's jaw.'

The Mouth-Breather's Jaw.—This deformity essentially involves the maxilla, the mandible being affected only in so far as its shape is moulded by that of its fellow. This fails to grow to its normal dimensions, and it is compressed laterally, so that the front portion projects unduly, while the palate is vaulted, and though actually less than the normal height, appears abnormally high.

The alveolar ridge being less than the normal length, while the teeth tend to grow to their normal dimensions, these are unable to take up their proper positions, and are thus irregularly disposed. *Pronounced dental irregularity, indeed, is pathognomonic of the mouth-breather's jaw*, and in nineteen cases out of twenty (like the mouth-breather's jaw itself), is indicative of the existence of adenoids, past or present.

Defective development of the maxilla leads to alteration in the shape not only of the mandible, but even of the skull.

Though adenoid disease is much the most frequent cause of nasal blockage in the young, and thus of the mouth-breather's jaw, children may, of course, suffer from nasal obstruction from other causes, so that a typical mouth-breather's jaw may sometimes be met with in a person who has never suffered from adenoids, but this is rare. Congenital syphilis, being a cause of nasal obstruction, may lead to the deformity; in this case, however, owing to the imperfect development of the teeth, dental irregularity is less apt to occur.

The pathology of this deformity has excited much controversy. Probably the chief factor in its production is a negative one—*i.e.*, the absence of the normal stimulus supplied by nasal breathing, Clearly, the daily passage of some fifty thousand respiratory currents through the nasal passages must influence the development of the surround-

ing parts. Another causative factor which has been suggested is the unduly low intranasal negative pressure produced by inspiration through partially obstructed nasal passages.

Pathology of Adenoids.—Adenoids is essentially a disease of civilized peoples. That it must be very rare among primitive communities is shown by the fact that among the vast collection of skulls of non-civilized races in the Hunterian Museum, the writer could not find a single mouth-breather's jaw.

One known factor in the production of adenoids is catarrh of the naso-pharynx, and this being often the result of microbic infection, the frequency of adenoids among the civilized may perhaps partly be explained by the frequency with which they suffer from infective 'colds in the head,' owing to their being so crowded together. There is, however, a much more potent cause of catarrh in children—namely, improper feeding, leading, as it does, to toxæmia of gastro-intestinal origin—'alimentary toxæmia,' as we may call it; improperly-fed children suffer greatly from gastritis, enteritis, bronchitis, pharyngitis, and rhinitis. The chief defect in the modern system of feeding children is that their food contains an excess of pultaceous starchy material, which both fails to afford sufficient exercise for the jaws and allows the stomach to be swamped with an excess of starch which has not been properly insalivated. In consequence of this, not only does the child suffer from perennial alimentary toxæmia, which renders him liable to catarrh, but the jaws and neighbouring parts, including the nasal apparatus, fail to develop properly. Now, an ill-developed naso-pharynx, lined by a catarrhally-disposed mucous membrane, affords conditions peculiarly favourable to the growth of adenoids. A further factor in causation is the absence of the normal stimulus to the flow of blood and lymph in this region afforded by vigorous mastication, the close proximity to the naso-pharynx of the powerful pterygoid muscles is worthy of note in this connection.

Adenoid disease is, in short, essentially a dietetic disease (H. Campbell), and might be practically eradicated by the adoption of a rational system of feeding children.

DISEASES OF THE TEETH.

The like is also true of most dental diseases—notably dental caries and pyorrhœa alveolaris, both of which might be greatly lessened by the adoption of a suitable diet.

The inhabitants of the United Kingdom have the worst teeth of any people in the world. There are upwards of 200 million carious teeth among them, and as many alveolar abscesses (pyorrhœa), in addition to many millions of root abscesses, practically the whole of which is preventable.

Dental Caries is due to the absorption of the enamel by the acids formed by the fermentation of starchy and sugary food which collects about the teeth.

Pyorrhœa alveolaris, or socket abscess (Rigg's disease), is a purulent inflammation of the periodontal membrane—*i.e.*, the periosteum lining the interior of the alveolus. This membrane becomes invaded with pyogenic cocci, and pus forms between it and the fang, causing the tooth to loosen, and ultimately to be shed.

It is a very prevalent disease in our own country. Practically the whole of the adult poor suffer from it, and a large proportion of the upper classes. It is essentially due to non-use of the teeth, the result of subsisting on a too soft vegetable food (animal food demands but little mastication), which fails adequately to stimulate the flow of blood and lymph in the buccal and periodontal membrane, or to elicit that copious flushing of the buccal cavity with the salivary secretions which adequate mastication induces. Vigorous mastication causes the teeth to execute a lively dance in their sockets, and by promoting the normal nutrition of the periodontal membrane increases their resistance to pyogenic invasion.

Root Abscess is an abscess which forms at the end of the fang of a dead tooth. The pus bores its way through the outer alveolar wall, and gives rise to a gumboil.

Civilization has been the means of vastly increasing the amount of disease in man. Especially has it increased the infectious diseases and those resulting from injudicious dietetic habits. The use of clothes and the congregation of large numbers of people in closed places has led to an

enormous increase of infectious disease, to which civilized man is by natural selection becoming increasingly immune. The cultivation and artificial preparation of vegetable food (to say nothing of the manufacture of alcoholic drinks) has had an equally important influence in increasing disease.

Preventative medicine has already done much to lessen the terrors of infectious disease—the greatest triumphs of medicine have, indeed, been in this field. Equally good results await the enforcement of proper dietetic methods.

SAPRÆMIA—SEPTICÆMIA—PYÆMIA.

The bacteria which, living on dead organic matter, cause putrefaction are known as *saprophytes* (*sapros*, putrid, rotten), and are described as *non-pathogenic*, because they are unable to grow on or in healthy living tissues. The bacteria which develop in living tissues are known as *parasites*, and are described as *pathogenic*.

Bacterial Products.—The most important of these are the *toxins*, which are the essential cause of the symptoms of bacterially-induced disease.

Sepsis.—This term is generally used in connection with wounds. A wound is said to be in a condition of *sepsis*, or to be *septic*, when it has become inoculated with pathogenic or non-pathogenic bacteria.

Infection is the term applied when pathogenic organisms, having entered the living body, develop therein.

Sapræmia, or Septic Intoxication.

If putrid blood-serum, or the fluid of decomposing tissue, is carefully *filtered* and injected into an animal, there result: rigor, pyrexia, muscular twitchings, vomiting, diarrhœa, and eventually, if the dose is sufficiently large, death from cardiac failure.

On examining the dead animal, the blood is found to be tarry and imperfectly coagulated, but *free from micro-organisms;* the endothelium of the heart and bloodvessels is stained by pigment derived from disintegrated chromocytes; small petechial hæmorrhages are noticed beneath the serous membranes; the lungs are engorged; the liver, spleen, and kidneys are soft, pulpy, and friable; and the intestinal mucous membrane is intensely congested.

The term *Sapræmia* is applied to the constitutional symptoms, similar to those just indicated, resulting from the absorption into the system of toxins generated by organisms, either pathogenic or non-pathogenic, existing in a septic wound. No organisms entering the body, the poison is not self-multiplying within the body, and its effects are strictly proportional to the dose absorbed. As found in man, examples are: Absorption of poisons from the pent-up discharges between the flaps of an amputation stump and the decomposed retained matter in the uterus after parturition.

Post-mortem Changes.—Death rarely results. The post-mortem changes are similar to those found after injecting putrid blood-serum in an animal (see above).

Septicæmia, or Septic Infection.

If *unfiltered* putrid fluid is injected into an animal, the result is the setting up of a train of symptoms very similar to those found in sapræmia; but the animal soon dies, even after very small injections, and *large numbers of micro-organisms are found in the blood.*

The term **Septicæmia** is applied to the condition which results from the entrance into the system of pathogenic organisms from a septic wound. The wound may be of the most trifling nature, but if it permits pathogenic organisms to enter, these may multiply in the system *ad infinitum*, and this being so, the symptoms are not proportional to the dose absorbed. In man septicæmia most frequently results from punctured, dissecting, and post-mortem wounds, and from infection during the puerperium. Most cases are due to streptococci.

Post-mortem Changes.—These are the same as those observed in sapræmia.

Pyæmia.

If a putrid fluid, holding in suspension not merely pathogenic micro-organisms, but decomposing solid particles, is injected into an animal, death takes place, and secondary abscesses are then found in the lungs, spleen, kidneys, and brain.

The term 'pyæmia' is applied to a condition similar to

the last, in which there occurs, in addition to the entrance of pathogenic micro-organisms, a passage of septic emboli into the blood-stream, giving rise to scattered abscesses. These emboli are derived from the breaking down of a septic thrombus in a vein, the sequence of events being—

Septic phlebitis in connection with a wound.

Inoculation of the contained thrombus with pathogenic organisms.

The breaking down of the thrombus into emboli.

Dissemination of the emboli by the circulation.

The plugging up of the terminal arterioles of the lungs, spleen, kidneys, etc., by such emboli.

The formation of infarcts, in which are reproduced the conditions existing in the original wound (=pyæmic abscesses).

The micro-organisms are the same as those found in septicæmia, streptococci being the most abundant.

Pyæmia was, in pre-Listerian days, a very common cause of death after operations and certain injuries, especially those implicating veins, bones, or joints; now it is but rarely seen, except in the form of *septic thrombosis of the lateral sinus* in connection with middle-ear disease.

Post-mortem Changes.—The *veins* leading from the infected wound show suppurative phlebitis and peri-phlebitis, and they contain thrombi in various stages of decomposition and disintegration.

The *lungs* are congested, and scattered throughout their substance are septic infarcts, ranging in size from a pea to a walnut, and having their bases beneath the pulmonary pleura. In the neighbourhood of the infarcts are patches of broncho-pneumonia. The pleural sacs contain a quantity of a dark-coloured turbid fluid mixed with pus.

The *heart muscle* is flabby, and often the seat of small abscesses. The pericardium may contain fluid similar to that found in the pleura. The interior of both the heart and the aorta is generally deeply stained with pigment derived from broken-down chromocytes.

The *liver*, *spleen*, *kidneys*, and *brain* usually show infarcts similar to those found in the lungs.

The *joints*, particularly those of the knee and shoulder, are often affected, and contain a thin purulent liquid.

Abscesses may form in other parts of the body, such as the parotid gland, and interior of the eye.

Portal pyæmia, or **suppurative pylephlebitis**, is that form of pyæmia which occurs in connection with ulceration of the gastro-intestinal tract or gall-bladder, or inflammation of the umbilical vein in newly-born infants. Multiple septic infarcts are found scattered throughout the liver, corresponding in situation to the terminal branches of the portal vein.

ANIMAL PARASITES.

Classification.

Protozoa	*Amœba coli.* *Entamœba histolytica.* *Trypanosoma.* *Malarial parasites.* *Treponema pallidum* *Leishman's body.*
Cestoda, or tape-worms	*Tænia solium.* *Tænia mediocanellata* *Tænia echinococcus.* *Bothriocephalus latus*
Nematoda, or thread-worms	*Ascaris lumbricoides.* *Oxyuris vermicularis.* *Trichocephalus dispar.* *Ankylostoma duodenale.* *Trichina spiralis.* *Filaria sanguinis hominis.* *Dracunculus medinensis.*
Trematoda, or fluke-worms	*Schistosomum*, or *Bilharzia hæmatobia.* *Schistosomum cattoi.* *Schistosomum japonicum.*

Protozoa.

The term *Protozoa* is applied to the lowest group of the animal kingdom, a group which is sharply distinguished from others (*Metazoa*) by the fact that its members are simple unicellular masses of protoplasm.

Amœba coli is found in the upper part of the large intestine; it does not penetrate the mucous membrane, and is probably quite harmless.

Entamœba histolytica is found in the dejecta and in the ulcers of the diseased bowel in Asiatic dysentery, also in the walls of a tropical abscess of the liver.

The organism measures 25 μ to 30 μ in diameter, and consists of an outer translucent part, the *ectosarc*, and an inner granular part, the *endosarc*. It is colourless, throws out pseudopodia, is actively motile, and in its general characters resembles the ordinary amœba. Reproduction is by fission.

Trypanosomata ' are minute protozoal organisms shaped like an elongated spindle, with a long lash or flagellum at one end, and a delicate finlike swimming membrane running from the attachment of the flagellum to the other end of the spindle. For the most part they are about the length, exclusive of the flagellum, of the diameter of a red corpuscle. They swim very actively in the blood-plasma, with a wriggling screwlike movement, the flagellum being usually in front ' (Manson).

One species, the *Trypanosoma Gambiense*, is probably the cause of that scourge of Africa, the *sleeping sickness* (in which disease there is a well-marked cerebro-spinal meningitis), as it is found in the blood, cerebro-spinal fluid, and lymphatic glands of patients suffering from this disease, being conveyed from the sick to the healthy by means of a biting fly—the *Glossina palpalis*. (Another fly, the *Glossina morsitans*, is now also suspected. It is found much farther south—as far as Rhodesia.)

Another species, the *Trypanosoma Brucei*, causes the tsetse-fly disease of horses, dogs, sheep, and the large game of Africa, the fly acting as the intermediary which carries the parasite from one mammal to another.

A third species, the *Trypanosoma Lewisi*, infests the rat.

Malarial Parasites.—Malarial fevers are caused by the presence in the blood of small protozoa, three species of which are found in the human body—benign tertian, malignant tertian, quartan. The parasite has two cycles of existence, one passed in man, the other in the mosquito. Into the human host the organism is introduced by the bite of the mosquito. Taking up its habitat in the red blood-corpuscles, it multiplies asexually by simple division. In addition to this method of asexual reproduction, the parasite also produces crescent-shaped sexual forms, which

under ordinary circumstances perish in the blood (being probably engulfed by phagocytes); but if they are transferred into the stomach of the mosquito, as when the insect bites a man whose blood contains these forms, they undergo further development there, and reproduce themselves sexually.

In the proboscis of the mosquito there are two separate tubes, one *up* which blood is sucked, the other *down* which the infected saliva is injected.

Of the three to four hundred described species of mosquito, only a limited number are malaria-carriers, and these belong to the subfamily *Anophelina*.

In common with other insects, the mosquito passes through the following stages of development: The adult female lays her eggs in *still* water. In the course of from two to four days these are hatched into *larvæ*, which in about ten days' time are transformed into the *pupæ*, these two days later becoming full-grown insects, or *imagos*. They then burst their pupa-cases, and fly away from the water.

The female anopheles alone is the blood-sucker.

The vitality and growth of the mosquito are favoured by warmth, and retarded, or altogether arrested, by cold.

The malarial parasite, once introduced into the blood of man, may persist for months, sometimes for a year or two. After this it dies out, unless reinfection by the mosquito takes place. Whilst in the blood, it lives entirely at the expense of the red corpuscles of its host.

The Human Cycle.—At the time of infection by the bite of the mosquito, minute rod shaped bodies—*sporozoites* (18) are introduced into the blood of the human host. Each sporozoite at once enters a red blood-corpuscle (1), in the interior of which it develops asexually in the following manner: The rod-shaped sporozoite assumes a spherical shape, forming a minute unicellular mass of protoplasm, *schizont* (2), exhibiting amœboid movement and occupying but a small part of the corpuscle. Gradually it increases in size until it occupies nearly the whole corpuscle (3), the hæmoglobin of which is converted into granules of pigment, which ultimately collect into clumps. The parasite now undergoes segmentation, arranging itself in a cluster of minute spherules, and forming what is known as the *rosette body* (4). This soon breaks

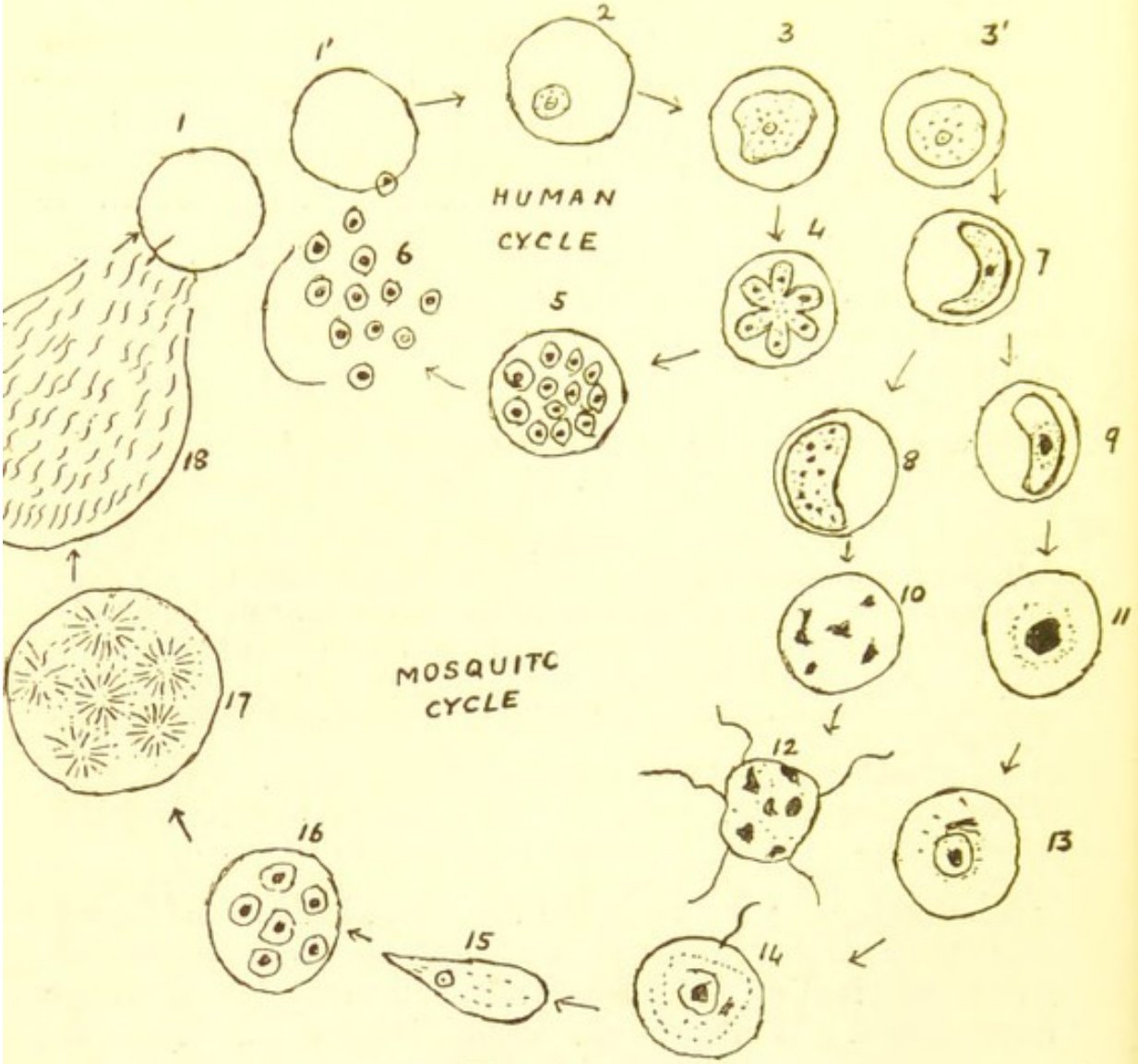

FIG. 17.

1, Red corpuscle with sporozoite entering; 1′, red corpuscle with merozoite entering; 2, 3, stages of development within red corpuscle (schizont); 4, rosette body; 5, formation of merozoites; 6, liberation of merozoites into plasma by bursting of red corpuscle; 3′, merozoite, which becomes (7) crescent body; 8, male crescent; 9, female crescent; 10, male gametocyte; 11, female gametocyte; 12, formation of microgametes in male gametocyte; 13, formation of macrogamete in female gametocyte; 14, fertilization of macrogamete of female gametocyte by a microgamete of the male gametocyte, which now becomes a zygote; 15, oökinet; 16, oöcyst; 17, development of sporoblasts; 18, liberation of sporozoites.

up into separate parts, *merozoites* (5), and by the end of forty-eight, or seventy-two hours, the corpuscle ruptures

and liberates these into the plasma (6). Each merozoite then invades a fresh red corpuscle (1), in which it repeats the same cycle of development.

This asexual process of multiplication by simple division is known as *schizogony*.

The setting free of the merozoites into the plasma coincides in time with the onset of the febrile attack, and it is probable that a fever-producing poison is also liberated when the corpuscle bursts.

The completion of this asexual cycle takes forty-eight hours in tertian fever, and seventy-two hours in quartan.

The Mosquito Cycle.—In addition to the above asexual multiplication, some of the parasites in the red corpuscles develop (as before explained) into crescent-shaped sexual forms (7).

The crescents contain pigment, and are of two distinct kinds : The *female crescent* (9), a long and narrow crescent, round the centre of which the pigment is arranged in a circle ; the *male crescent* (8), a shorter and thicker crescent, throughout which the pigment is scattered irregularly.

Each of these bodies remains enclosed within the thin shell of its respective red blood-corpuscle, and if left in the blood of man undergoes no further development. Should, however, a mosquito bite a person in whose blood these crescents exist, they are then conveyed into the insect's stomach, and there, escaping from the red blood-corpuscles, become free.

The crescents now become spherical, and are known as the female (11) and male (10) *gametocytes* respectively. From the outside of the male gametocyte (12) whiplike filaments (*microgametes*) now protrude, and becoming detached, swim about in the stomach of the mosquito until, meeting a female gametocyte (13), one of them fertilizes the large cell (*macrogamete*) contained in it (14), and gives rise to a *zygote*.

The zygote, at first spherical, becomes ovoid with a pointed end (*oökinet*, 15), and, acquiring powers of locomotion, burrows through the epithelial lining of the stomach, and comes to rest between the epithelial and the muscular layers.

Here it forms a capsule round itself, becomes spherical

and begins to grow (*oöcyst*, 16), until by the end of from ten to fourteen days it has attained a comparatively large size. 'During this time the contents have become converted into a number of rounded masses (*sporoblasts*, 17), each of which, when the process of subdivision is completed, becomes covered with a pile of thickly-set, minute, elongated, spindle-shaped rods (*sporozoites*, 18), arranged like the spines on a hedgehog' (Manson). Finally, the capsule ruptures, and the sporozoites, escaping into the lymphatics on the outer surface of the stomach, enter the circulation, and are ultimately conveyed to the salivary gland. When the mosquito bites a man, the sporozoites travel down the proboscis with the salivary or poison fluid and are injected into their human host (1), and there meeting red blood cells, function as merozoites did.

Varieties of human malaria:

1. *Benign tertian* (the common form).
2. *Malignant tertian.*
3. *Quartan.*

Summary of Sexual Cycle.

The *female gametocyte* encloses a single cell, called the *macrogamete*, which is the homologue of the ovum.

The *male gametocyte* develops upon its exterior whiplike processes, called *microgametes*, which are the homologue of the spermatozoa.

One of these microgametes fertilizes a macrogamete, the result being a *zygote*.

The zygote, when it has acquired powers of locomotion, is termed an *oökinet*. The encysted oökinet in the stomach wall is called an *oöcyst*.

In the oöcyst are developed the *sporoblasts*, and from these finally are formed the *sporozoites*.

Treponema Pallidum.—*Vide* p. 176.

Leishman's bodies (or **Leishman-Donovan**) are found in the spleen and bone-marrow of tropical splenomegaly, or *kala-azar*. Each is ovoid in outline, with a large deeply staining nucleus, and a tiny rod-shaped, still more deeply staining nucleolus.

Species: *Leishman-Donovani*, causes kala-azar (India); *Leishman tropica*, causes Delhi boil; *Leishman infantum*, causes infantile splenic anæmia.

Cestoda (*kestos,* a girdle).

The members of this group have a life-history which is peculiar in that it embraces two distinct stages of existence —the *adult stage,* generally found in one species of animals (the host), and the *embryonic stage,* found usually in another species (the intermediate host).

The adult tape-worm occupies the intestines. It consists of a head, a narrow neck, and a series of flattened segments, or *proglottides.*

The head at its widest part is provided with four suckers, by means of which it fastens itself to the intestinal mucous membrane of the host, and anteriorly it is prolonged into a *rostellum,* or proboscis, surrounded by two rows of hooklets.

Commencing at the anterior part of the body and running backwards along each side are two longitudinal tubes—the *water vascular system.* There is no alimentary canal.

Each proglottis is bisexual, the respective sexual ducts opening at the genital papilla, which is placed at one edge of each proglottis, the papillæ being at alternate sides of successive segments.

The *testes* consist of small vesicles, the ducts of which unite into a vas deferens, which enters the penis.

The *uterus* is branched, having a central canal with lateral diverticula, and being connected at one end with *two ovaries* by means of two oviducts, and at the other end with a vagina. The spermatozoa travel from the penis, enter the vagina at the genital pore, and then fertilize the ova. The distal proglottides, holding the embryos, become detached, and escape from the intestines with the fæces.

The proglottis then decomposes and liberates the embryos, each of which is provided with six hooks and surrounded by a capsule. If the embryos are now swallowed by another animal (*the intermediate host*), their capsules are dissolved by its digestive juices, and the embryos escape into the alimentary canal of the new host. They then bore their way through the walls of the alimentary canal, and finally settle in the viscera, or the muscles. After this, the further development of the embryo is as follows: The hooklets disappear, and at the caudal end a cavity develops, in the interior of which an

immature head (*scolex*) appears, the whole organism being afterwards enclosed by a fibrous capsule formed by condensation of the surrounding connective tissues of the host. This intermediate stage is known as the *Cysticercus cellulosæ*, or bladder-worm. Should the flesh of the animal harbouring the *Cysticercus cellulosæ* now be consumed by another animal, the head of the cysticercus becomes everted, and, losing its bladder-like appendage, fastens itself to the intestine of the new host by means of its four suckers, and develops proglottides from its caudal end.

Hydatid Cyst.—The intermediate stage of the *Tænia echinococcus* is known as the hydatid. The embryos,

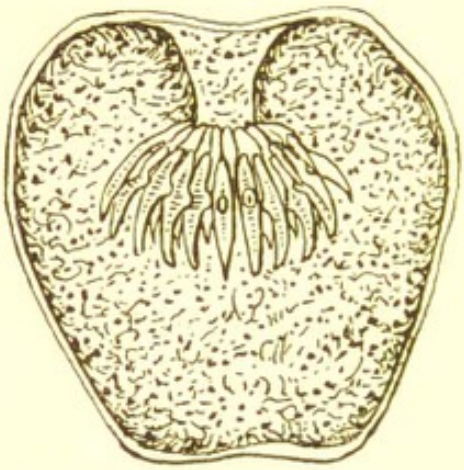

FIG. 18.—BROOD CAPSULE.

provided with their six hooks, enter the alimentary canal of some animal—say man—and their capsules being dissolved by the digestive juices of the host, they are set free. They then bore their way into the tributaries of the portal vein, and so reach the liver or other organ, where they come to rest.

Each embryo now loses its hooklets, and is converted into a cyst, the walls of which are composed of concentric laminæ lined by granular cells—the *germinal membrane*—and filled with a non-albuminous fluid rich in sodium chloride and containing the hooklets, which are of great diagnostic value. They are insoluble in acids. Within the cyst are *brood capsules;* these are small vesicles which, originating from the germinal membrane, contain

immature heads (*scolices*) crowned with hooklets, and are analogous to the *Cysticercus cellulosæ* of the other tape-worms.

The entire hydatid cyst is surrounded by an adventitious capsule of fibrous tissue.

TABLE OF CHIEF POINTS CONCERNING THE TAPE-WORMS.

Name.	Tænia solium.	Tænia mediocanellata.	Tænia echinococcus.	Bothriocephalus latus.
Length	10 feet	15 feet	¼ inch	20 feet
Proglottides ...	800	1,000	3, exclusive of head	3,500
Head	$\frac{1}{24}$ inch	$\frac{1}{12}$ inch	$\frac{1}{36}$ inch	$\frac{1}{10}$ inch
Rostellum ...	present	absent	present	absent
Hooklets	26	absent	present	absent
Suckers	4	4	4	2
Intermediate host	Pig	Ox	Man and sheep	Sturgeon, pike, trout

N.B.—*Average* length and number of proglottides given.

Nematoda (*nema*, a thread).

These are slender, elongated worms tapering at the extremities. Each has an alimentary canal, with mouth and anus. The sexes are distinct, the female being the larger. A few typical members of the class alone need be described.

Ankylostoma Duodenale. — The female is about ½ inch in length, the male slightly shorter. The mouth is furnished with teeth, by which the worm fastens itself to the duodenal mucous membrane of the host. The egg is enclosed within a thin transparent capsule, and is voided with the fæces. It then matures in damp earth, the embryos invading the body of the new host, probably by penetrating the skin, generally that of the feet or legs.

From the skin they enter the blood, ultimately reaching the lungs. Up to this time they retain their original size,

but once in the air-passages of the lungs their growth is rapid. They then travel up from the air-vesicles into the bronchi, trachea, and glottis, whence they pass into the œsophagus, and thence into the duodenum, where they attain maturity.

These parasites, in virtue of their leechlike habits, suck a great quantity of blood from the duodenal mucous membrane, causing a serious form of anæmia (*coolie anæmia*), which is associated with a great increase in the eosinophile leucocytes in the blood. The worm in 1906 made its appearance amongst the miners engaged in the Dalcoath tin-mine in Cornwall. It is common in Egypt, Brazil, Italy, and other hot countries.

Trichina Spiralis.—The female is about $\frac{1}{8}$ inch long, and the male about $\frac{1}{12}$ inch. The mature worm is found in the intestines of man and other animals; the immature form is found in the muscles. The ova are hatched into embryos in the uterus, *the young being born in the free state.* The life-history of this parasite is as follows: When infected pork, *e.g.*, is eaten, the capsules containing the embryos are dissolved in the stomach by the digestive juices, and the liberated young worms pass into the intestines. Here, in the course of a few days, they attain maturity and pair, the females afterwards boring their way through the mucous membrane into the lymphatics, where they liberate their young (each female giving birth to thousands), which are then carried into the general circulation. Ultimately they reach the voluntary muscles (especially the abdominal, thoracic, pharyngeal, and tongue), and piercing the sarcolemma, coil themselves up in the interior of the fibres, and become encysted, in this position undergoing no further development until the infected flesh is eaten by a new host. After a time the cyst wall may calcify. The cysts are visible to the naked eye as minute white specks, first observed by Sir James Paget, when a student in the dissecting-room of St. Bartholomew's Hospital.

They have been found in all striated muscle except that of the heart.

The disease is conveyed to man by the ingestion of imperfectly cooked trichinosed pork. The pig is usually infected by eating trichinosed rats.

Filaria Sanguinis Hominis.—The adult form of this worm is known as the *Filaria Bancrofti*, and the embryonic form as the *Filaria nocturna*.

Filaria Bancrofti.—This form is confined to the lymphatics. The female is about $3\frac{1}{2}$ inches long, the male only about half this size.

Reproduction is viviparous, the female discharging her embryos into the lymph, by which they are carried into the blood-stream by way of the thoracic duct.

Filaria Nocturna.—The snakelike embryo is about $\frac{1}{90}$ of an inch long, its breadth about the diameter of a red blood-corpuscle. The head is provided with a short spine, and a circlet of hooked lips.

The organism is imprisoned within a long loose sac, inside which it can be seen to wriggle, but from which it is powerless to escape, so long as it remains in its human host.

The embryos are present in the surface bloodvessels during sleeping hours only—whence the name *F. nocturna;* when the patient awakes they gradually retire to the lungs and larger bloodvessels. The cause of this remarkable periodicity is unknown. If a filarial patient changes his hours of sleep from night to day, the periodicity changes correspondingly.

As these filariæ cannot further develop in the human host, they probably soon die, unless they are removed to an intermediate host. This latter is a species of mosquito (*Culex fastigans*), which swallows the filaria when sucking human blood. In the mosquito's stomach the embryo escapes from the sac which has hitherto enclosed it, and bores its way through to the thoracic muscles, where it comes to rest. By about four weeks' time it has grown considerably, and then, resuming its travels, it reaches the proboscis, and returns to another human host when the insect stings. It now passes to the lymphatics, where it matures into the *Filaria Bancrofti.* The sexes then come together, and the young are born.

Filariasis.—In the large majority of cases the presence of filariæ in the human body gives rise to no obvious symptoms. Occasionally, however, the mature worm may block the lymphatics, or the female may discharge, instead of embryos, unhatched ova which are large enough

to obstruct the lymph-stream, and so give rise to *lymph-stasis*. When this happens, any of the following tropical diseases may result:

Chyluria, due to ruptured lymphatics in the urinary tract, the urine becoming milky in appearance and coagulating into a jelly after standing. Analogous conditions are—

Chylous diarrhœa.
Chylous ascites.

Lymph scrotum, characterized by the presence in the scrotum of dilated and varicose lymphatics; these sometimes burst.

Elephantiasis Arabum, characterized by hypertrophy of the tissues, the result of blocked lymphatics. It is most commonly met with in the legs and genitals. Enormous tumours may thus form, the scrotum, for instance, alone having been known to weigh as much as 100 pounds.

Varicose lymphatic glands, giving rise to soft, painless tumours, over which the skin can be freely moved.

Abscesses, from the irritation caused by blocked lymphatics or by dead filariæ.

In addition to the *Filaria Bancrofti* and its embryonic form, *Filaria nocturna*, which are found all over the tropics, there are at least three other allied species found in the tropics—viz., *Filaria diurna* (West Africa), *Filaria perstans* (Africa and Demerara), and *Filaria demarquai* (West Indies and Demerara).

Trematoda.

The only member of this group at all common in man is the *Bilharzia hæmatobia*. The parasite is found in Natal, the Transvaal, Egypt, Madagascar, and the West Indies (particularly Porto Rico).

The female worm is about 1 inch long, the male about ½ inch. They inhabit the portal vein and its tributaries, also the vesical veins.

The ventral surface of the male is concave, and during copulation the lateral borders become infolded so as to enclose the female in a 'gynæcophoric canal.' The ova are shaped like melon-seeds, being provided at the pointed end with a spine, by means of which they work their way

through the walls of the small veins; they thus gain entrance into the rectum or bladder, whence they are discharged with the fæces and urine. A good deal of oozing of blood from the mucous surfaces may be caused by the migration.

The ova cannot mature whilst in the body, but if placed in water, or if the urine containing them be diluted with water, the capsules then burst, and the ciliated embryos are set free.

As regards the intermediate host nothing is known. Analogy with the history of the other nematodes would suggest that the embryo enters some fresh-water animal, in whose body it undergoes a further developmental change. Infection in man is probably through drinking contaminated water. Some maintain that the embryos enter the urethra or anus during the act of bathing.

The effect of the parasite is to cause *endemic hæmaturia*, as also the passage of blood from the rectum. Condylomata may develop both inside and outside the anus, and for this reason the case may be mistaken for syphilis.

The period of incubation which elapses between infection and the appearance of ova in the urine, would appear to exceed four months.

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[illegible] most characteristic — sudden
[illegible] acutely ill for a week. Then
crisis over & temp & patient becomes
mal.

b. 1st change in lungs — congestion
[illegible] dull, heavy & dark purple color. Does
[illegible] on thumb.

2nd Red hepatization: suppurating
exudate with abscess. Structure resembles
[illegible] Cut surface dry
3rd Stage — Gray hepatization. Color
[illegible] now instead of Red.
Cut surface wet.
[illegible] exudate — fibrin, polymorphonuclear leucocytes
[illegible] R. B. C. shrinkage of exudate &
[illegible] spaces around them.

[illegible] Resolution if case going to get better
Polymorphonuclear pneumococci
[illegible] removed by enzymes & absorbed into B. S.
[illegible] the [illegible] antibodies

pg 224 - 226

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