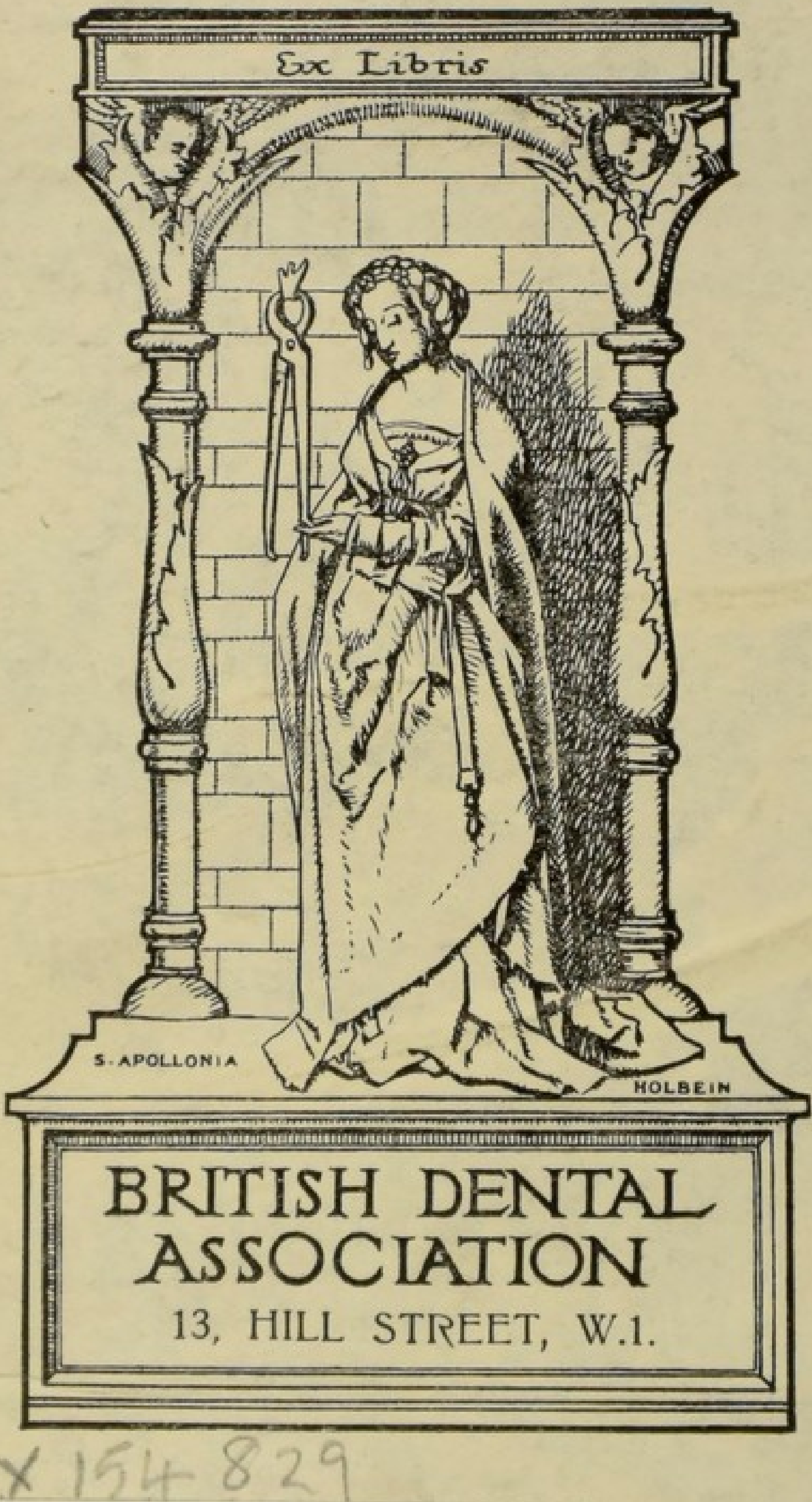
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STUDENT'S HANDBOOK OF COMPARATIVE PATHOLOGY.

STUDIES

IN

HUMAN AND COMPARATIVE PATHOLOGY

BY

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&c., &c.

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To

ROSWELL PARK

IN GRATEFUL APPRECIATION OF HIS SERVICES

TO COMPARATIVE PATHOLOGY.

PREFACE.

While the Study of Comparative Pathology is as yet in its infancy, it may perhaps not be thought premature to bring before the Profession, the results of some investigations in this direction, trusting that their practical interest and their suggestions may in some measure atone for their incompleteness.

The field which must be covered is so enormously wide, embracing at least the three distinct and usually separated provinces of Morphology, Veterinary Medicine and Human Pathology, that the only hope of successful development lies in the combined activities of myriads of observers.

When to this is added the fact, that pathological material from the lower animals, excepting in one or two domestic species, is both scarce and hard to procure, then some of the difficulties which stand in the way of anything like a complete treatment of the subject will be apparent.

The object of this little volume is twofold. First, to outline the facts already accumulated in this new field, so that they might be easily seen, in a brief but comprehensive way, by the student and be appreciable at a glance by the busy practitioner. Secondly, to endeavour to convince the Profession at large, of the high practical interest and value of the study and point of view, so as to enlist their coöperation in its further pursuit.

No specialist in any one line of study can hope to secure a sufficiently extensive series of data for safe conclusions. This can only be done by the registering of observations and collection of specimens by a hundred wide-awake and interested workers in every corner of the field.

My brief experience has already convinced me that the widest and most fruitful opportunities for this sort of work are those possessed by the practising physician, both human and veterinary, especially in the country.

To this end the treatment of the subject has been made of the broadest and most suggestive, many tentative positions being taken merely as a basis for, and indication of, a line of further investigation.

The effort has been rather to stimulate thought and investigation in others, than to advance dogmatic conclusions based upon any researches of my own.

Covering as the work does such a number of separate provinces of study, it is inevitable that conclusions will have been drawn, which to experts in the particular subject, will seem to be unwarranted, and that some errors of statement will have crept in, for both of which, forbearance is asked in advance.

My original intention had been to prepare a larger and more complete Memoir, fully illustrated; but a demand unexpectedly arising for a Student's Handbook upon the subject, the present outline-form was adopted.

The work has unfortunately been done under the influence of indifferent health. My most cordial thanks are due to the Editor, Dr. EDWARD BLAKE, who has rendered most ungrudging and invaluable assistance in the preparation of the book from its beginning. My complete physical breakdown necessitated my return to the United States and subsequent removal to the Pacific Slope, when only the earlier chapters were in type, the list of references not having been made out.

From that time Dr. BLAKE most kindly undertook entire charge of the publication.

In the gathering of data and material, so numerous have been the courtesies shown and so varied the sources of valued assistance, that it seems almost invidious to particularize by the mention of names.

I am however especially and most gratefully indebted to the Faculty of the University of Buffalo, both for their generous enterprise in maintaining a line of research in this new and untried field and also for their liberality in granting leave of absence for study abroad.

To the Council and Officers of the Zoological Society of London generally, but more particularly to the Vice-secretary, Mr. F. E. BEDDARD, I am under deep and lasting obligations, not alone for the superb facilities for study, but also for the collection of specimens so generously afforded me in the Prosector's Laboratory at the Gardens.

Among my veterinarian friends, my thanks for much valued information and courteous assistance are especially due to Prof. JAMES of Cornell University, to Dr. EBERLEIN of the Royal Veterinary School of Berlin and to Prof. J. MacFadyean of the Royal Veterinarian College, London.

The painstaking kindness of Dr. FERNIE of Folkestone, in volunteering to compile the excellent Index, is most gratefully appreciated.

The Author also begs to cordially acknowledge indebtedness to the kindly and intelligent coöperation of both publisher and printer, who have done their utmost in every way to make the book a success.

NEWBERG, OREGON.
November, 1900.

SYNOPSIS.

ILLUSTRATIONS.

STUDIES IN HUMAN AND COMPARATIVE PATHOLOGY.

CHAPTER I.

The Cell-Republic, and the Individuality of the Cell in Health and in Disease.

Ever since the establishment of the cellular theory of disease by the father of modern pathology, the body has been conceived of as a "cell-state" or "cell-republic" composed of myriads of plastid "citizens." And like other democracies, its government both in health and disease is recognised to be, to adapt Lincoln's celebrated phrase, "of the cells, by the cells, and for the cells." And although the citizen-cells were at first regarded as but little better than local sub-divisions of the tissue, bricks in the body-wall, cogs in the vital machine, they have slowly but steadily come to be recognised as the ultimate forces, and so far as we may apply psychic terms to their activities, the controlling and directing power of the body-politic.

And I venture the opinion that even yet the cellular theory of disease is not "cellular" enough, does not sufficiently recognise the individuality, the independence, the power of initiative of the single cell. Too often it still assumes that because a cell has, in specialising itself, lost some of its original powers and its freedom of action, it has, therefore, ceased to be an individual, and that its activities have become mechanical in place of vital.

Nothing could be further from the fact, and I firmly believe that our clearest insight into and grasp upon the problems of pathology in the future will come from a recognition of the essential independence, vitality, and if we may again be permitted a psychic term, "personality" of the individual cells of even our most narrowly and rigidly specialised tissues. Although the vast majority of their life activities are in and for the service of the entire organism, yet they are quite capable at times, as for instance in cancer and sarcoma, of sharply reversing this relation and using the nutritive fluids of the body for their own over-growth in such proportions as to imperil and even destroy the entire organism, by the toxins which result from their early decay. It can hardly be questioned that the *rôle* of some of the most useful and apparently subordinate groups of cells, as for instance those of the intestinal epithelium, is really as much excretory from their standpoint as it is secretory from that of the organism. In other words, that we are really living in part upon the waste products of some of our own cells.

In short, the "citizens" of our cell-republic are true democrats, loyal and long-suffering, but jealous of their rights; capable indeed of asserting them if badly treated, even to the extent of fatal rebellion.

First of all, let us pass in rapid review the various specialisations which have taken place in and among the cells of the different tissue groups, in order to estimate to what extent the striking modifications, which many of them have undergone, are still consistent with the retention of individuality and independence. Secondly, whether such specialisations can be paralleled by actually separate and independent organisms existing in animal communities outside the body.

Beginning with that great class whose vitality is reduced to the lowest level and whose departure from the "self-supporting" type is widest, the bone-corpuscles in their calcareous matrix, we find a group whose chief use to the body apparently lies in the heavy, stone-like masses of lime "concrete" which they have deposited around their processes and between their bodies. And yet even as leverage-bars and protection-plates the bones are far more than mere masses of lime-stone, knit together and toughened by a fibrous network. Walled up as the bone-cells literally are, each in a calcareous prison of his own making, they are still emphatically alive, and upon the maintenance of a fair degree of vigour and vitality in them, depends the strength and resisting power of the entire mass, although they form less than a third of it. Destroy their vitality, and the bone will waste away before the growth of granulation-tissue, dissolve in the fluids of the body, or snap across under the slightest strain. Moreover, they display powers of repair after fracture or injury as extensive as almost any other tissue-cells in the body, and indeed in the perfection of their rebuilding powers they excel all. So little is this form of specialisation-change inconsistent with the preservation of individualism, that we actually find its precise counterpart outside of the organised body in the familiar process of coral-building. The coralpolyp precipitates around its ectoderm and along its septa, the lime-salts of the sea-water, just as the bone-corpuscle does those of the blood and lymph. A coral-reef is simply one of the ribs of a continent.

Next in order comes the familiar *connective-tissue* group, the cells of which, though degraded, have retained more of their vitality. The irritability and motility of their original protoplasm has been lost in the formation of tough, stringy bands to support and bind together the more delicate tissues. Being more alive, it is also capable of greater activity both biologic and pathologic. In many respects purely mechanical in its supporting and binding functions, it still retains considerable powers of growth and of change. Largely through its activity is carried out that marvel of animal physiology, the process of repair. By the fatty transformation of the protoplasm of its cells, the surplus food materials of times of plenty are stored away against times of stress and scarcity. Whatever defect of the body tissues may occur, it is always prompt to fill the gap. And of course its power for evil is as distinguished as its power for good. Its cells give rise to the whole group of mesoblastic tumours and new growths, from the dangerous sarcoma to the innocent lipoma, the tubercle and the gumma. Its mere formation in excess produces that most widely spread and most serious of all degenerations, arterio-capillary fibrosis, whether cerebral, renal or cardiac.

And again it is accurately matched, outside of the organised body, by the branching fibres of the familiar sponge and its colonies. Although, of course, it must be remembered that in both these cases some fibrous tissues are the result of an external deposit by the cells, rather than of a direct transformation of their own protoplasm *in situ*.

Next in order, and in reality forming a slightly divergent branch of the binding group, we have the great class of storage tissues, the fat cells. Their function is to absorb all the surplus food material in the body, and forming it first into protoplasm, to allow this to break down in their own interior into droplets of a yellow hydro-carbon, which has the advantage of being capable of storage for considerable periods. Although great activity seems to be shown in the appropriation of this material, yet it is loosely held and entirely at the disposal of the organism as a whole, for in fever or starvation these droplets are the first element in our body mass to be burned up and disappear, leaving the fat cell gaunt and shrunken and scarcely to be distinguished from his building-stuff neighbours. In fact, we have much ground for the belief that once rid of its fatty contents, it becomes again not only structurally, but functionally, identical with the connective-tissue corpuscle and possessed of all its powers.

And this form of specialisation has also its parallel outside of the body in one of the classes of the communities of a species of Mexican ant, whose distinguishing feature is an enormously distended œsophagus, capable of containing treble the weight of the entire remainder of the body. They are neither soldiers nor labourers, but they accompany the latter on their honey-gathering excursions, and as the spoils are collected they are literally packed full of sweets by the workers. When extended to their utmost capacity they fall into a sort of "hibernating" condition, are then carried into the ant-hill and hung up by the hind legs in chambers specially prepared for the purpose, in which, we trust, enjoyable state and position they are left until their contents are needed for the consumption of the community, when they are waked up, made to disgorge and resume their ordinary life activities till next season's honey-gathering begins. So considerable is the amount of honey stored in one of these insects that the Indians take pains to collect them from the ant-hills and eat them as a dessert. In fact, they were mistaken for fruit, and described as "small golden-yellow gooseberries of honey-like sweetness" by the early Spanish explorers.

Another most important group of worker-cells is the blood corpuscles, which maintain their independence and freedom to a more evident degree than any other class

Nowhere are the solidarity and the *esprit de corps* that exist between all the body cells more strikingly shown. The blood cells, both red and white, live in the plasma stream, which flows through the channels of the body, just as their ancestor, the amœba, lived in the water of the sluggish ditch. They are rolled along in its throbbing stream by the contractions of the great heart-pump, apparently precisely as so many pebbles or rubber balls might be. There is absolutely no sign of connection that can be detected even by the highest immersion lens, between any of them and the other cells of the body, not even with the telegraph-like nervous system. Such apparent "free-lances" are they, that one or two early observers ventured upon the quaint suggestion that they appear to be some sort of extraneous organism which has become a domesticated parasite or useful dependent of the body system. And yet with all this absolute freedom and apparent "detachedness," there is absolutely no group of cells in the body which so instantly responds to every demand for assistance on the part of the other cells. They are in fact the literal mounted police and light skirmishers of the entire organism, and are sent hurrying to the front by the thousand, like the other "thin red line" of British infantry at the Battle of Waterloo, the instant that injury occurs or is even threatened. Long before the drowsy fixed cells have really awakened to the danger which threatens them, and have got ready to depart from the peaceful monotony of their usual existence, these little red- and white-coated Cossacks of the body standing-army have begun to redden the horizon from every direction and hurl themselves in solid masses upon the invader.

Of course, a large part of the movements of the red cells can be accounted for by the mechanism of the heart and blood-vessels. They are simply poured through the blood-channels like grains of wheat in an elevator, or pebbles in the bed of a stream. But the behaviour of the white cells goes far beyond this. Not only do all those, circulating normally in the vessels of the injured part, promptly adhere to the intima, work their way through the wall and crowd the tissue spaces, but as has been announced by Ehrlich and confirmed by Cabot's recent studies in leucocytosis, all which are "feeding" in the lymph channels, serous cavities and tissue-spaces of the rest of the body, make their way into the blood-stream and pour toward the site of danger. Hence the marked and extraordinarily rapid leucocytosis which follows pus-formation anywhere in the body. Arrived at the seat of war, the free cells promptly attack such bacteria as may be present, absorb broken-down materials, assist in the formation of callus, or in other processes of repair. If the bacilli and their toxins can be promptly destroyed by them, resolution occurs, if not, then the cells die and disintegrate, and pus is formed. In all this the marvel is that, although so completely detached and independent, they are so intensely loyal and vitally useful.

And if we were to inquire upon what does their peculiar value to the body-politic chiefly depend, we should find that it was the extent to which they have retained their primitive, ancestral characters. They are formed in the lymph-nodes, which are merely little islands of tissue of embryonic type, preserved in the body chiefly as breeding-grounds for cells of this primitive type. They are literally the Indian police, the scavengers of the entire organism. They have the roving habits and the fighting instincts of the savage. But it would also seem as if, like the savage, they can only be depended upon for "police" or "skirmish" work. In the resistance to the great systemic fevers, the chief and ultimate brunt falls upon the burgher-like fixed cells of the body. And I believe that upon the proportional relation between these primitive and specialised cells of our body-group, between the light horse and the pikemen, as it were, will be found to depend many of those singular differences, not only of degree, but of kind, in the immunity possessed by various individuals. While some surgeons or anatomists will have a temperature from the merest scratch, and yet either never develop any serious infection or display very high resisting power in the later stages, others will stand forty slight inoculations with absolute impunity, and yet when once the leucocyte barrier is broken down, will make apparently little resistance to a fatal systemic infection.

And these, of course, are only a few out of a score of ways in which the leucocytes live and die for the "Fatherland." Our whole alimentary canal is continually patrolled by them, poured into it by the tonsils above and the patches of Peyer below. Were it not for these, we should be continually in danger of poisoning by the products of our own intestinal processes. It seems probable that it is only when the toxic processes, taking place in the alimentary canal, get beyond the control of the patches of Peyer, that we get the systemic symptoms of that often fatal intoxication, typhoid fever. At least the succession of changes in these glands in typhoid corresponds, first, to excessive production of free phagocytes; second, to crowding of the gland-mesh with imperfectly developed lymph-cells unable apparently to "get themselves born" and detached; lastly, to necrosis from pressure, ulceration and perforation or hæmorrhage. While, as will be considered in a later chapter, in infancy and childhood, when these glands are nearly twice as numerous and active as in adult life, typhoid is rare, and if present, mild in form; whilst in old age, when they have almost disappeared, it is extremely fatal.

I need not remind you that the production of fibrin, the formation of the blood-clot, and all the wonderful powers of healing and protection to the body which that process implies, are dependent chiefly upon the sacrifice of the leucocyte. In fact, these "enslaved amœbæ" of ours are among our most useful citizens, and yet their individuality, independence and power of initiative are strikingly complete and not the least element in their value to the body politic. The strikingly altruistic transformation which they possibly undergo into the higher form of the red cell, whether it be by the loss of their nuclei and sacrifice of their powers of reproduction, or by the bursting of their cell-wall and scattering of their chromatin granules, is an equally wonderful process, and will be considered at length in our discussion of the anemias from the cell standpoint.

Last, but not least, come the great group of epithelial citizen-cells, with their three great lines of specialisation, the protective, the secretive, and the responsive. The first of these, as illustrated in the skin and its appendages—the hair and nails, is apparently the most mechanical of any; and yet the more carefully we watch any of these classes of appendages, in health and in disease, the more we are impressed with the dependence of their effectiveness upon the vitality and vigour of their constituent cells. The dependence of the health of the skin upon abundance of air, of friction and of its natural ancestral life-medium, cold water, is a thing to which all our dermatologists are steadily coming to bear unanimous testimony. The same may be said of the hair,—keep it thoroughly *alive* and half its disturbances disappear at once. In the secretive division, we have the most extraordinary degree of individual skill and intelligence developed that is to be found. Just those elements which are needed for their nutrition are picked out from the food-mass and all alike are transmuted into that precise chemical compound which will be of the greatest advantage to the organism as a whole. Although the action of the responsive class is more wonderful at first sight, especially in the ganglion cells, yet the more we study it, the more obviously automatic it becomes. In all three classes it is a simple refinement upon some of the powers possessed by the primitive ancestral cell which forms the core of their wonderful effectiveness.

And here we have a strikingly similar parallel in those other less firmly-welded animal communities, the colonies of Hydroids, bees and ants. In a clump of Hydroids, for instance, we find from two to three distinct classes of "persons" or individual cells. Some whose tips are expanded into blunt mushroom-like processes, with thick leathery skin and even with thorny or spike-like epidermal projections upon them, whose function, as seen when the group is attacked or irritated, is to serve as a sort of living *chevaux de frise* behind which the sensitive and secretive individuals of the colony may hide themselves. Another set of "persons" will be distinguished by long, tentacle-like prolongations of their protoplasm, often tipped with an abundance of cilia, floating out in the water beyond the limits of the other persons of the colony. They are wide awake to give notice of the approach of danger or the proximity of food. One class of these is particularly well-armed with the lasso-cells or stinging-threads with which either to secure prey or repel attack. Last of all, we have the comparatively unspecialised, thick, cup-like secretive "persons" of the community, whose use it is to eat up the materials secured by the more active members and turn them to account in the process of reproduction. Among the bees and the ants, we have a somewhat similar specialisation of a worker class of sexless females who are at the same time the fighting element; the nutritive person, the queen, who is also the reproductive individual for the entire colony; and the purely male-reproductive individual, the drone, who is supported and tolerated by the community until his function in this respect has been accomplished. While among the ants we have a distinct military class, a worker class, a storage class of "honey-pots," and a sort of "special-sense" class, whose business it appears to be to keep continually on scouting duty. As in the hive, our "worker-class" and fighting class seem to be so closely united as to be almost indistinguishable, and the wonderful contractile cell of our muscle-tissue is both of these in one; yes, and the farmer class as well, for it seems probable, that in the crucible of his stomach are performed nearly all the ultimate processes of the body metabolism. The teeth may masticate, the tongue may swallow, the stomach may elaborate, and the liver may metamorphose the food materials of the body, but the real eating of the same is done in the stomachs of the muscle-cells, and here, and here alone, is the true birthplace of appetite. Is it any wonder that "*Exercise*, EXERCISE, EXERCISE," is rapidly becoming recognised as our most potent remedy in all sorts of morbid conditions?

To sum up. The citizens of the Cell Republic, our body, retain most of their rights in full, whilst they reserve the remainder *in posse*. They all assimilate and secrete and *fight;* even the "absorptive" processes, so-called, of the cells of the alimentary mucous membrane are vital activities, as the loop-isolation experiments of several observers have proved. All are irritable, although they do not exercise their power in this respect in some classes, except under the stress of disease, as, for instance, the bone-cells in osteo-myelitis, the cartilage cells, which, destitute of nerves as they are, can be goaded into agony in acute arthritis, and the curiously undifferentiated cells of the tooth-pulp, in which some of our histologists assure us no distinct neurons or neuraxons can be distinguished. All are contractile, even, as Golgi has shown, the neurons of the medullated fibres. So that the nerve-impulse is literally a ball, thrown from hand to hand, not a mere electric current through a wire. They all reproduce their kind, the ease and facility of this process being in inverse ratio to the degree of their specialisation, from the bacteria-like fecundity of the white blood-cell, up to the slow and difficult parturition of the nerve- or muscle-cell.

Another thing, which I think we are apt to forget, is the extent to which this specialisation is carried out "upon the spur of the moment," as it were, and in immediate response to the environment. Heredity, of course, plays a wonderful part, but we cannot too clearly bear in mind that all, even of our most highly specialised cells, are emphatically of local origin; they are the "products of home industries," they may be markedly increased or decreased in number or proportion, or even created *de novo* under the pressure of immediate need. Our bones, for instance, rigid and enduring as they are, and following such similar lines in every individual organism as to have given rise to the utterly false and misleading position, both in teaching and practice, that they are literally the foundation of the body, upon which all other tissues are moulded, are really simply the *hardened core* of the different segments of the arches and appendages of which the body is composed. And their limits advance or retreat in response to the muscular strain upon them, as is beautifully shown by the parallel variations between the angle of the jaw and the vigour of the masseter at different ages. Joints, developmentally, are mere solutions of continuity in this hardened core, and the synovia a primitive slime poured out by the embryonic tissue surrounding their cavities. The primitive nature of the joint tissues is shown from another point of view by their peculiar liability, in early life, to the attack of the tubercle bacillus, and in later life to the toxins of rheumatism and gout.

The blood-vessels themselves are formed, in any given area, either simply by an orderly arrangement of the embryonic cells to coat or line cavities, reaching in certain directions through the tissues, or by the actual hollowing out of the bodies of the cells which arrange themselves in loops or radiating lines through the area. Every cell of the endothelial wall of the capillaries is to be regarded as of local origin and a part of the tissues in which it is embedded, with immediate power of responding to their needs, of arresting the white cells upon its surface or of pouring out a stream of serum through its substance in response to their demands. Even the nerve-cells may be seen educating themselves, as it were, and specialising themselves into existence in every area of rapid growth, hypertrophy or neoplasm, their occurrence in the later situation having been most interestingly demonstrated within the last few months by the researches of Hugh Young,* and this, too, in some cases in situations where they apparently did not connect with the general nervous system of the body, but were needed only for the internal economy of the tumour.

The more carefully we study the action of any organ or tissue, the more continually we are confronted with this individual vital activity of the constituent cells as one of the chief factors in its metabolism. For instance, in the process of food and liquid absorption from the alimentary canal, the filtration-osmosis theory is utterly

* *Journal of Experimental Medicine*, Jan., 1897.

inadequate. The chief and most difficult products of digestion, for instance, the peptones, have almost totally disappeared before the portal vein is reached. Not only this but a solution of the peptones or of the contents of the small intestine during digestion, injected into the blood of an animal, acts as a powerful poison. The highest powers of our lenses have been used in vain in the effort to discover the interspaces between the cells covering the villi, through which the fat-globules made their way into the lacteals, and the fact that they must pass through the muscular (mucosa) coating being usually entirely ignored. Now, however, that it has been observed in the hedgehog, and several lower vertebrates and invertebrates, that the fixed cells of the epithelial lining of the canal can actually be seen during digestion to thrust out pseudopodic processes and engulf the food particles in regular amœboid fashion, it begins to dawn upon us that we probably have here to do with a genuine eating, digesting, and "excreting-upon-the-other-side" process, on the part of even these closely packed and orderly-looking cells. It seems more than probable that the orderly, pavement-like arrangement of these cells with their even ranks and uniform surface, as seen in the ordinary section, is a purely post-mortem condition, and about as accurately represents their shape and condition in life, as the alignment of a regiment on dress-parade does its appearance in the skirmish-line or upon the field of battle. Humiliating as the fact may appear, it even seems highly probable that the rest of the cells of our body are living upon what we politely term the results of the metabolism of the cells of our alimentary epithelium, but which would in plain English be quite as accurately termed their waste-products.

The wonderful rhythm of the heart-beat, upon which every instant of our existence depends, is at the bottom due to the independent activity of the cells composing its walls, and is simply *regulated* and controlled by the vagus and sympathetic nerves. The same may be said also of that rhythmic contraction in the muscle-coat of the smaller arterioles, and probably also in the primitive endothelial cells of the walls of the capillaries themselves, which, as the great skin-heart, furnishes probably a considerable proportion of the motor power of the circulation. No rational explanation of the phenomena of stasis and inflammation is possible which does not take into account the local origin, sympathy, and individual action of the cell-walls of the capillaries of any given area. Mere dilatation of their lumen or rise of blood-pressure is utterly inadequate to account for even the simplest forms of hyperæmia and stasis. As Wesley Mills has suggested, from the point of view of comparative pathology, the capillaries are to be regarded as glands which secrete blood serum for the particular area in which they lie.

The same thing is true in the so-called excretory processes, as, for instance, in the glomeruli and tubules of the kidney, which, so far from acting as so much filter paper, actually pick out and feed upon the precedents of both urea and uric acid, and form a large part of those substances in their interior and excrete them on the other side, so to speak, into the tubules. Anything which lowers the nutrition or impairs the vitality of these cells leads to the accumulation of waste-products in the blood, but, as has been proved time and again, *not* of urea or uric acid. And a toxic, impoverished or overladen condition of the blood, the lowering or the increase of pressure in the kidney, will alike produce the symptoms of what we are pleased to term "uræmia." As to the independence of the ganglion-cell or the cell of the cortex, probably more has been said than the actual facts will justify, but the individuality of that mere telegraph-wire, the medullated nerve-fibre, has only just been conclusively demonstrated; thus the extraordinary simulation-pareses, anæsthesias, and amblyopias of hysteria and of neurasthenia are for the first time satisfactorily explained by the contractility of those neurons which form the "wire."

Nor is this individual activity by any means always confined to directions which are of advantage to the individual cell. Many a cell in the body, performs its highest functions not by its life, but by its death; as the death of the molecule is the life of the cell, so the death of the cell, in many cases, is the life of the body, and the death of the body, the life of the race. Take the epithelium of the mammary gland, for instance, which subserves the purposes of the body by breaking up its protoplasm into fat-globules, then dying and scattering them abroad in the milk-serum. Next, the continual drying down and shedding of the scaly epithelium of our body-surface, by which both our secretions and any foreign bodies which may lodge upon our surface are shed continually outward. Thus our silky, waterproof, external coating, flexible as silk, but resistant as steel-mail to the entrance of noxious organisms or materials is kept up. The behaviour of our leucocytes in the presence of bacteria, and a score of other instances will suggest themselves.

Not only have our individual cells both volition and independence, but they also have "memory." As will be discussed later, some of the most frequent morbid processes and extraordinary departures from the normal rhythm, are simply the repetition, on the part of the cells, of processes which were normal in a now almost forgotten ancestry. The hairs which grow upon the buccal epithelium, the pyloric hairs in the stomachs of certain birds, the hair and teeth of dermoid cysts, will serve as illustrations. With all their independence and individualism, the tone, as it were, of the entire body is one of harmony, of loyalty and devotion to a degree which is seldom equalled—never excelled,—in the external human community. But, in view of these facts, is it any wonder that departures from this rule will sometimes occur? The marvel is that they do not happen more frequently.

We must always remember that the one right which the free citizen prizes, in ultimate resort, above all others, is that of rebellion. When we come to investigate the ultimate cause of a large proportion of our disease processes, we shall find that an exercise of this right, upon the part of certain groups of cells or "tissues," seems the underlying factor in the process. Our whole group of tumours, for instance, are cases in point. As in most rebellions, their dangerousness will be found to depend largely upon the degree of misgovernment and the extent to which vital rights are disregarded on the part of the central power. Put any part of the tissues of the body upon inadequate rations, by the cutting off of local supplies, formerly issued, which we term the process of atrophy, as in the mammary gland, or in the uterus after the child-bearing period, and you find the cells of the tissue or organ ready to assume the right of initiative in the form of a sarcoma or a cancer.

In fine, disease, in eight cases out of ten, will be found to be traceable to a neglect of, or denial to, some class of our citizen-cells of their "rights to life, liberty, and the pursuit of happiness," figuratively speaking.

If the following conclusions may not legitimately be drawn from a hasty survey of our conceptions of the organisation of the body politic; they may at least be submitted as a basis for discussion in later chapters.

(1) That the term "Disease" is a purely relative one.

(2) That it would appear to consist chiefly of a vital, and even from a "cell" point of view, healthful process on the part of some cell or tissue group, which is out of harmony with the balance of the activities of the entire organism.

(3) That *morbid* activity is at bottom *healthy* activity gone wrong,—life out of place.

(4) That the processes of disease pursue an orderly succession, and are subject to laws which may be studied and ascertained.

(5) That pathology is simply a branch of biology. And finally, as will be made the principal burden of our theme, that disease has not merely a natural history, but an ancestry of its own. Indeed, in many cases, it will be found to be a revelation of the ancestral history of the tissue or organ in which it occurs.

CHAPTER II

The Diseases of the Alimentary Canal: The Stomach.

The study of pedigrees is of peculiar interest. Not only does it throw valuable light upon the past, but it often helps us to forecast the future, or at least to estimate the balance of probabilities. And it is upon such estimates solely that most of our decisions either in medicine or affairs must be based. Believing that the history of the growth of the food-tube in the past, is an important key to its probable behaviour in the future, my purpose in this chapter is first to hastily glance over the course of its development, trite as it may be to many, and then to take up the question whether this course has any bearing upon its disease-tendencies in its present form? Are any of its morbid disturbances simply exaggerations or deficiencies of its normal growth-tendencies?

The earliest appearance of anything which could be dignified with the name of a stomach is found, of course, in the amœba. It consists simply of a dipping or pouching-in of any part of its surface, which happens to come in contact with a food-morsel. The cell literally engulfs the edible particle, partly by allowing it to sink into its semi-fluid mass, and partly by flowing out in pseudopodia upon all sides of it, until the processes meet and enclose it. The stomach is a dimple, deepening into a pouch. When all the soluble elements of the "meal" have been extracted, the pseudopodia slowly flow apart, the pouch becomes open again, and the amœba gently glides back on either side, while the undigested remnants are swept away by the same currents that brought them there. In fact, the organ is an impromptu, and can be improvised at a moment's notice on any part of the amœba's surface; and this is the typical form of stomach in the protozoa. Absolutely simple as the device is, it has its advantages: if one part of the surface become "dyspeptic," a new one can be utilised; two or three different food-masses can be accommodated at once, without even waiting for a mouth to be emptied. No such thing as gastritis is to be feared, for should the food-matters prove not easy of digestion or irritating, the pseudopodia can flow back on either hand, the pouch is opened and the offending materials quietly set afloat again in the ditch-water. Our boasted superiority to our ancestors sometimes brings penalties with it.

In the *Polyzoa* the organ first attains the dignity of a permanent institution. Here, as in the hydra, for instance, it becomes a simple, tubular bag or pouch, round which the rest of the organism arranges itself—merely a part of the general surface which having been tucked in for digestive purposes, has remained so, as it were. It has, of course, a mouth with a row of cilia or tentacles round it, but few other details of any importance. In the higher members of the group, such as the sea anemone, the mouth of the bag becomes deeply grooved on either side, and by the aid of cilia, a "down-current" is established in one of these grooves, and an "up-current" in the other, so that the food goes down on one side and the excreta are returned upon the other. If we picture this tendency to increase until the two grooves become separated as by the falling together of the lips of the gastrula-mouth, the primitive bag would be changed into a U-shaped tube, with two openings lying comparatively close together. In worms the "U" gets straightened out, as it were, and we have the primitive alimentary canal, a simple tube of almost uniform calibre, running straight from one end of the body to the other. From this onwards, it is simply a question of dilatation of this portion and coiling of that, till we reach the very highest form of the organ in our cousins, the herbivora.

These swellings and coilings, although ultimately resulting in a very elaborate structure, are originally of the simplest possible character. In all cases they will be found to depend directly upon the digestive and alimentary needs of the forms to which they belong. They are simply a response of internal conditions to external demands, the external condition, in this case, being, for the most part, the nature of the food supply. In the great groups of *Insects* and *Crustacea*, these changes consist almost entirely of certain biting, grasping, and crushing mechanisms, mostly in the forms of rings or arches about the anterior opening of the tube, and one or more enlargements, somewhere in its anterior third for the delay and moistening of the food, usually followed by a second crushing mechanism or "mill" of the gizzard type, the remainder of the canal continuing almost straight and of uniform calibre directly back to the anus.

And thus the canal enters the *Vertebrate* sub-kingdom. In the lower species of fishes it still consists mainly of simple tube, the anterior part of which is considerably dilated for the obvious purpose of permitting the prey to be swallowed whole. At the beginning of about its middle third this dilated part of the canal takes a somewhat sudden bend upon itself, much after the fashion of an old-fashioned German tobacco-pipe, after which it rapidly tapers down again to what might be regarded as its primitive calibre, and pursues its course to the anus in a direction varying from almost a straight line in some of the lower forms, such as the gar-pike, to the formation of two or three simple loops in the true bony fishes. Its average length is scarcely more than once and a half to twice the length of the body of the animal, and this, of course, is obviously correlated with the almost purely carnivorous habits of the fish and the readily soluble nature of the flesh upon which it lives. The canal of the fish is constructed on the principle of being just adequate to engulf the food, retain it until absorption can take place, and then discharge it as promptly as possible. And this same principle will explain the construction of even the highest forms of the alimentary canal.

In *Reptiles* much the same condition of affairs exists, except that the canal behind the stomach is somewhat longer and more elaborately coiled, owing, apparently, to the less soluble nature of their food, which still consists of flesh. In *Birds* we find a distinct step forward in the the line of complexity. A special dilatation is found in front of the stomach, in the course of the gullet, known as the crop, where the soaking and macerating of the food materials take place, and a reappearance of the old ancestral crustacean and vermian "gastric mill" or mechanism for crushing the food, in the stomach proper, in the shape of the well-known gizzard, which occupies a position corresponding to the pylorus and pyloric region of the mammalian stomach. All of these are also curious reproductions of the alimentary arrangements in the higher insects. The intestine has also become considerably elongated and in consequence coiled, so as to accommodate itself to the body cavity. It is also beginning to show signs of division into a small and large portion. In *Mammals*, of course, we have the familiar condition of a large mouth cavity, but, as the prey is no longer swallowed entire, a small gullet, an expansion of varying size known as the stomach, a more or less elaborately elongated and coiled portion for absorptive purposes, the small intestine, and a curiously puckered or sacculated large intestine and tubular rectum. The range of variation in these comparatively simple specialisations is, however, enormous, harmonising in every case with the primitive keynote of the nature of the food and the conditions under which it must be digested.

The typical carnivorous canal, for instance, with its moderate-sized, pear-shaped distension for a stomach, its simple coils of small intestine, its small cæcum and short large intestine, measuring only from three to six times the length of the body, is obviously the fish food-tube modified for the purpose of attacking flesh instead of fish. At the other extreme, the enormously-ballooned and many-chambered gastric pouch, the long and complicated small intestine, the huge cæcum and colon of the herbivora, reaching a length of from twelve to twenty times that of the body of the animal, is a striking illustration of immensely increased elaborateness, in order to contend with a food of much greater bulk and correspondingly difficult digestion. The cæco-appendix alone in some of these forms may be twice the length of the body—a greater proportional length than the entire alimentary canal in some lower species.

While this development of the main calibre of the tube has been going on, a number of important appendages, or off-shoots, have been springing up, in the shape of little pouches or pockets budding out from the wall of the canal at certain convenient points. By a further course of budding and rebudding forming ultimately the more or less elaborate glands which secrete the ferments and juices needed in the various digestive processes. There are several pairs of salivary glands which bud out from the sides of the mouth-part of the tube; the thymus and thyroid, which are given off from its upper third; the numerous tubular buddings just beyond the pyloric region, which ultimately result in the massive liver on the one side and the pancreas on the other; and, finally, the little air-bladder which sprouts out from the ventral aspect of the gullet and enlarges to form the lungs—all of them the result of that simple but wonderfully adaptable process of pouching or invaginating by which the stomach itself, in the amœba and in the hydra was originally formed. Indeed, it might be said, in passing, that the nervous system, the muscles, the skeleton, and the special senses will be found either growing directly out from this wonderful little tube or in response to some of its demands. In fact, the best definition, from a morphological standpoint, that has been given of a man is "a stomach and its appendages."

When we turn to the individual life-history of the human stomach, we find it simply a striking epitome of its ancestral history. Beginning probably as a dimple upon the surface of the mulberry mass, changing rapidly to a thimble-like pouch or cup in the gastrula, from this to a simple longitudinal tube, only partially closed. This tube, first of all, shows a flexion and slight dilatation for the stomach, next a dipping-in of the epiderm to form a mouth (stomodæum), later still a similar dipping-in (proctodæum) at the caudal end to form the anus, then the occurrence of coils in the hitherto straight intestine, and finally the outgrowth of a large segment between this and the rectum, which is often not properly adjusted in its final position and moorings even at birth.

So much for the double pedigree. Now let us see if we can find any connection between this and the behaviour of the canal in health and disease. The thing that strikes us first of all is that the stomach part of the canal is actually undergoing some of these changes during the life of the individual. The stomach of the infant at birth is often but little more than a simple, almost spindle-shaped dilatation, followed by a hook-like curvature, in the course of the primitive canal. It was discovered practically, a number of years ago, that its capacity in proportion to the body was much smaller than that in the adult; and more careful investigations have made this discrepancy even greater, until Rotch declares, in his latest paper, that what might be termed the comfortable or normal capacity of the human stomach at birth, is scarcely five-sixths of an ounce. It has almost no fundus, and in consequence can reject its contents with an ease and promptness familiar to all. In fact, an infant stomach is practically still in the fish stage; and to the morphologist the *a priori* suggestion would be extremely strong, simply from a study of its form and relative development, that the organism required a purely carnivorous diet and the flesh material in a highly soluble form.

There has probably been no single improvement in dietetics which has resulted in greater increase of comfort and vigour to the human race than the practical recognition of this morphological fact, that the human infant is emphatically and essentially carnivorous in its tastes, and can live and flourish properly on no other kind of food. The abolition of "paps" and gruels and puddings of every sort and description, and the substitution of an absolute milk diet, or, if this fails, meat juices, during the first six months of life, has done simply wonders for the comfort and nutrition of the race, and been the chief factor in the enormous lowering of infant mortality. And even in young ruminants the stomach corresponds with surprising closeness to the natural suckling diet. Although all the four divisions of the organ are present and it is much larger than in a carnivore of the same weight, yet while the last or "true" stomach in the adult is barely a tenth of the capacity of the first or paunch, in the newborn calf or lamb it is almost as large as the other three put together.

Professor Law, of Cornell University, the well-known veterinarian, informs me that in his opinion young calves during the suckling period have a distinctly higher resisting power against certain diseases, *e.g.* anthrax and tuberculosis, which resembles the immunity possessed by carnivora against these diseases, and is in part due to their carnivorous diet. And that repeated experiments upon foxes and rats have shown that the resistance of these animals to various infections was heightened by a flesh diet and markedly lowered by a vegetable one.

As the child grows the salivary glands begin to secrete, the jaws become armed with teeth, food that requires some grinding is indicated, and the stomach adjusts itself along with the other organs. The change from this to the adult stage is largely one of increase in capacity and development of fundus, and the assumption of a somewhat more horizontal or, more accurately, oblique position. So far as its form is concerned, it is apparently simply a sort of swelling or sagging process which is taking place. In fact, as we watch it, the conviction forces itself upon us that it is to a large degree a form of storage-pouch or receptacle, in which food may be retained, moistened, churned somewhat and then passed on for real digestion and absorption to the remaining part of the canal. And we are told now by a certain school of modern physiological experimenters, that the stomach is little better than a sort of alimentary tub and churn. It is true, the fluid which is poured out for the moistening of the food contains certain amounts of pepsin and hydrochloric acid; but that, instead of being a rare feat, is now known to be a comparatively common power not merely of animal, but of vegetable tissue. The layer of cells, which surround the germ in a grain of corn, when sprouting is about to occur, attacks the tough cellulose and fibrous husk, which cover the grain, by means of a fluid, rich in pepsin, which the cells secrete. The cells about the base of the "eye" of the potato, use the same weapon in dissolving the cellulose coating of the starch-grains, in order that they may be made available for the nutrition of the young sprout. And even such lowly organised forms as some of the fungi, attack the tissues of the plants upon which they feed by means of a pepsin ferment which is secreted about the tips of their hyphæ.

The chemical changes, which take place in the food while in the stomach, are of unquestioned importance, yet we cannot help thinking that the mechanical changes, such as the softening and churning and subdividing, are much more so. And if this be true, as its history of growth would imply, it is at bottom essentially a muscular organ rather than a glandular one. Certain it is that the greater part of the true digestive processes and all absorption take place in the intestine, with its much more powerful juices. Digestion can be perfectly carried out where the stomach is completely excluded by ligature or otherwise, and the ingenious researches of Meltzer* and others have recently shown that, where the pylorus is firmly ligated, not only no food-absorption, but positively no water-absorption, takes place in the stomach, so that even potent and diffusible poisons like strychnine and atropine can be introduced into such a stomach and retained there for hours, without producing any toxic effects upon the system.

And this view of the situation is supported in a really remarkable manner by the latest results of our gastric therapeutics. The use of the lavage-tube, the test-meal, and the gastroscope, has revealed the fact that the most serious and unmanageable defect which can occur in the organ is loss of motor power, either through distension or otherwise. So long as the stomach is able to empty its contents into the intestine with reasonable promptness, digestion may be well performed and nutrition maintained in spite of most serious defects in the quality and quantity of the gastric ferments. In fact, the most characteristic and fundamental feature of the majority of the chronic forms of gastric disturbance is this inability on the part of the stomach to empty itself, and little or no permanent benefit will be derived from treatment until this defect is remedied. As in any other muscular organ, the loss of motor power is the most serious defect which can occur in it.

* Transactions, Association of American Physicians, 1896.

But will our ancestral history allow us to throw any light upon the reason or method of loss of this motor power? We think it will, and that in quite a direct manner. In the vast majority of cases this loss of motor power is attended, and indeed often caused, by an excessive distension of the walls of the organ, either by the retained food or by the gases developing from its fermentation, so as to stretch and thin out not only the muscular, but even the mucous and glandular coat, to the point of atrophy. Now, this fact of distension is no new thing. In reality, it is simply a continuation of the very same process of enlargement in response to the needs of the organism and the nature of the food, which we have been tracing from the simplest forms of the organ. Like nearly all other diseases, it is a healthy process gone wrong, a beneficial change carried to excess and become harmful in the process. In fact, to use a very loose simile, the carnivorous human stomach has undergone enlargement to a most herbivorous size.

Indeed, in some cases the parallel may be a very close one, for under the use of certain kinds of food in healthy individuals, or by narrowing of the pylorus, the stomach may be greatly enlarged without any loss of motor power; undergo a genuine hypertrophy, in fact, instead of a dilatation, just as may its sister-organ, the heart. The enlargement is the same in either case, but in the one case the organ has responded to the stimulus and its muscular wall kept pace with the increase in size, while in the other case it has been conquered by the stimulus, and its power to dilate has proved its ruin.

The connection between form and disease-tendencies, appears to obtain among the lower animals also. The simple pear-shaped stomach of the dog, so closely resembling our own, has almost precisely the same disease-tendencies. Catarrh and catarrhal gastritis are quite common; and, from almost identical causes, bad food, overloading, chills, infections, etc., but run a mild and rapid course, and are usually recovered from. The stomach can be promptly and easily emptied by vomiting, whenever its contents are or become irritating, and, although the disease may become chronic, yet it is seldom severe, and little true dilatation occurs.

In the horse, ox and sheep, however, acute indigestion and gastritis, while somewhat less common, owing to a less irritating character of food, are far more serious in their results. They are extremely apt to become chronic, and fatal symptoms develop with great rapidity. The reason for this in the horse, with his comparatively small and simple stomach, appears to be the great difficulty in vomiting. This is due in part to the length of the œsophagus below the diaphragm, but chiefly to the extraordinarily oblique direction in which the œsophagus opens into the stomach. It almost seems to run between the layers of the muscular coat for some distance before debouching, like the ureter does between the coats of the bladder. Even after death one has great difficulty in forcing a bougie or large probe through the œsophageal opening from the lumen of the gullet, and vomiting is almost impossible; when it does occur, the horse sits down on his haunches like a dog, and it is regarded as a symptom of grave and probably fatal import.

In the ox and sheep the many chambers and great size of the organ furnish an obvious cause. Retention and stagnation of the food-contents is so easy that even the slightest gastritis or indigestion may result seriously. A certain degree of safety-valve action seems to be furnished by the habit of rumination, or returning the food for a second mastication, when, if found unpalatable, it can be rejected. However, unfortunately, almost the first effect of fermentation or irritation is to stop rumination, the cow "loses her cud," in popular phraseology—a phrase which is accepted with absolute literalness and various substances are thrust into the animal's mouth "to make a new cud"—and the fermenting mass of grain and grass pours off quantities of gas which, trapped in the huge blind sac of the paunch, distends it with frightful rapidity. The extent and fatality of this distension are almost incredible. The huge four-chambered stomach balloons out until it not only fills the entire abdominal cavity, but causes the left flank to bulge out and up so that it reaches the level of the spinous processes of the vertebral column. So tremendous becomes the pressure upon the lungs and heart, as in even our own feeble imitation of the process, that death may actually occur by asphyxia, or by apoplexy due to interference with the return of blood to the right heart, and congestion or rupture of the cerebral capillaries. Rupture of the stomach-wall and fatal peritonitis is not at all uncommon, and even the diaphragm itself has frequently been known to rupture under the tremendous pressure. The suddenness of the process is appalling, death by any of these causes may actually occur in from half an hour to three hours; in severe cases and most fatal attacks, the end comes within a few hours, and the mortality of untreated cases is extremely high.

The gas which produces all this disturbance is chiefly carbonic oxide (74 per cent.) and carburet of hydrogen (24 per cent.). Every extreme specialisation brings its own special danger with it. The very size of the herbivorous stomach becomes its fatal weakness. Tympanites is almost unknown in the dog and the pig, with their simple stomachs; it is also very rare in birds. In some 300 autopsies at the Zoological Gardens, I have never once found it in a bird, nor in a carnivore, but not infrequently in deer and antelopes, and occasionally in kangaroos and monkeys, though never to the bovine degree. That it is the pressure of gas which causes the most serious symptoms is shown by the prompt relief afforded by puncturing, with a trocar, the bulging paunch in the left flank, the most effective treatment in cattle. The influence of the mere shape and size of the paunch, is illustrated by the fact that the calf, in which, as we have already seen, this is the smaller part of the stomach, is exempt from the disease, in all but its mildest form.

Even the occurrence of gastric ulcers seems to be influenced in some degree by the form of the stomach. These, though always rare, are most frequent in the dog and curiously in the calf (whose gastric disturbances are almost identical with those of the carnivora), where they present the familiar "peptic" type. In the herbivora, with their much less acid and active gastric juice, this form of ulcer is almost unknown. Gastric ulcerations in these, are usually due either to thromboses occurring in the course of the exanthemata, typhoid and other fevers, or to foreign bodies, which are easily taken in, in the large bulks of food required, and find great difficulty in escaping from the paunch. Frequently they end by piercing its wall and imbedding themselves in the surrounding viscera and tissues, especially the pericardium.

There are two other pathological tendencies of the tract which, I cannot help thinking, have some ancestral basis, remote as it may seem. One is the extraordinary power, possessed by the walls of the stomach, of both secreting and absorbing gases of various kinds, particularly air and carbon dioxide. Only a part of the gases present in many cases of gastric distension can be accounted for by the fermentation of the food contents Clinicians were for a long time puzzled to account for their presence, and for the rapidity with which they would be renewed after their escape had been arranged for. They were driven to the conclusion, in fact, that the mucous membrane of the stomach must have the power of absorbing the gases from the blood in its walls. When we remember that the primitive alimentary tract performed, in all the stages of its development, previous to the appearance of gills, the functions not only of digestion and absorption, but also of respiration, and that the mammalian lung is simply a part of the common alimentary tract set apart for this special purpose, we can, I think, gain some notion of how easy it would be for any part of the tube to resume this ancestral function. And when we further recall that this power of respiring gases may exercise itself upon the sulphuretted hydrogen and other poisonous products of intestinal putrefaction, we can readily understand the influence, in the production of anæmias and toxæmias of every description, exerted by stagnation of the food contents.

The other is that extraordinary sympathy which still seems to exist between the alimentary mucous membrane and the epithelium of the body surface, from which it was originally pouched or tucked in, if we may use the expression. This is most commonly shown in some forms of the common "cold," or coryza, in which serious disturbances of the gastric and intestinal mucous membrane, and even of the epithelium of the liver and pancreas, derived therefrom, follow a marked interference with the cutaneous circulation. The so-called "bilious attacks" which follow a cold, or the "gastric form" of *la grippe*, are cases in point. A striking illustration is the appearance of urea in the stomach in Bright's disease, in some cases of which a diagnosis of renal inadequacy can be made merely from a chemical examination of the vomited matters. And I cannot help thinking that those mysterious ulcers of the duodenum, which are so apt to occur after extensive burns of the surface, are an aberrant expression of this same primeval sympathy.

That the stomach was literally the mother of all the other organs of the body, we have living proof every day in the remarkable degree to which it remains a sympathising centre for disturbances in every part of the system. Ranging all the way from the nausea of fear, the "yearning of the bowels" of pity, the "bleeding a man into his own (portal) blood-vessels" which underlies alike fainting and surgical shock, up to the gastric anacidity of astigmatism, the "crises" of *tabes dorsalis*, and the dyspepsia of lithæmia. Not inaptly did our shrewd old forefathers in the art call the solar plexus and its branches the "sympathetic" nervous system.

The more carefully the stomach is studied by specialists such as Ewald, Boaz, Osler, Glenard, and Stockton, the more clearly the conclusion seems to be reached that a large proportion of its disturbances are chiefly vibrations in response to chords struck in some other and often distant part of the system. The last-mentioned, indeed, declares, with that breadth of view characteristic of all his work and so often lacking in the vision of the modern specialist, that *sixty per cent.* of gastric disturbances *have their origin outside of the stomach.*

In fact, I believe I am justified in claiming that the correlation between phylogenetic age and physiological stability holds even here, and that the stomach, as the oldest organ of the body, is also, considering its exposed position and highly vital function, one of the least frequently diseased. Most of the disturbances usually ascribed to it are either reflexes (whether nutritional or nervous) from some other organ, or are due to direct irritation from poisonous or indigestible ingesta. No other organ of equal vital rank is so seldom found to be the site of actual lesions after death. Lung, liver, heart, kidneys, and even brain and genito-urinary tract are all higher up on the post-mortem list than the stomach. Carcinoma, ulcers, and atrophy due to distension would almost complete the roll of its anatomical changes.

CHAPTER III.

Diseases of the Intestine: Colic; Appendicitis; Parasites.

When we come to consider the diseases of the intestine, both small and large, the relation between history and morbid tendencies is less obvious. Partly because specialization has been less marked and has proceeded for the most part only in one direction. But even here there seems to be some sort of connection between the direction taken by the ancestral tendency of change and the form of disturbance to which this part of the canal is most liable. Almost the whole change which has taken place in the small intestine, from the primitive straight, simple tube, consists of an increase in length, accompanied by a corresponding increase in the number of coils and loops, and it is this very tendency which we find to be a peculiar source of danger in this region. The various twists and knots which are so liable to occur in this part of the bowel are simply an exaggeration of the coiling tendency which its normal history has shown; and the tremendous propulsive power which its great increase in length and comparatively small increase in calibre has necessitated (a motor power which will be appreciated and highly valued by any one who has attempted to clean of their contents five or ten coils of a cat's intestine), this powerful vermicular action is the essential factor in the production of that most serious and distressing condition, intussusception. The bowel literally turns that energy, which has been developed in propelling the food along its enormously extended tract, to swallowing a part of itself.

Nor has this power of lengthening its absorptive surface in response to food demands ceased at birth in the human species. The ingenious researches of Marfan* upon the bodies of rickety children have shown that their well known "pot-belly" is chiefly due to a marked lengthening of the entire intestine, which, instead of being the normal length, six times that of the body, reached eight, nine, and even *ten* times this length. An almost identical state of affairs was found in dyspeptic children, and as Marfan acutely suggests, it is probable that a similar elongation underlies many cases of enteroptosis in adults. In both these classes it is a response to imperfect absorption, as in other races—*e. g.*, the negro—to coarse and indigestible food. Its greater length in cattle and horses appears to render it more liable to intussusception than in the dog and pig, and also to volvulus and intestinal calculi. In all families, we find abundance of acute enteritis, due to fevers, bad food or water, parasites, etc. An interesting feature of this disease, in both the horse and ox, is the readiness with which Peyer's patches undergo inflammation and suppuration, followed by atrophy, so that many febrile diseases accompanied by enteritis have erroneously been described as "typhoid" of the horse and of the ox. The former is now known to be a form of influenza, and the latter an acute myco-enteritis due to mouldy fodder. A similar but less marked susceptibility in the dog and pig has led to the same confusion of names, most of the group designated as "typhoid" in both having been since traced to ptomaine-poisoning by diseased or putrid meat.

* "Revue Nou. des Maladies de L'Enfance," Feb., 1895.

So far all attempts to inoculate animals with human typhoid have entirely failed. So completely may the glands be destroyed in the ox, that on post-mortem examination their situation will be found to be occupied by punched-out ulcers, or in recovered cases by smooth depressed scars.

And it is a curious coincidence that in childhood when the patches of Peyer are nearly twice as numerous as in the adult, typhoid fever is extremely rare, although the glands readily become swollen and inflamed. While in old age, when the glands have almost entirely disappeared, typhoid though rare is extremely fatal. Which suggests that susceptibility to typhoid depends largely upon the inadequacy of the phagocyte-breeding function of the agminate glands.

One broad distinction may be laid down between the symptoms of enteritis in herbivora and in carnivora. This is, that as a rule—to which of course there are many exceptions—both acute, and severe forms of chronic, enteritis are accompanied by constipation in the former and diarrhœa or dysentery in the latter, and here again the mixed feeder and the suckling ruminant behave as carnivora, as is well illustrated in pigs, calves, and lambs. Birds also, with their much shorter intestine, are far more liable to diarrhœa than to constipation; in fact it would appear as if the longer the canal—and consequent delay of the food—the more difficulty it has in emptying itself promptly.

A large proportion of intestinal inflammations in animals are due to toxic ingesta; poisonous plants and moulds upon fodder, in herbivora; and decaying meat or fish in the carnivora; food-poisonings of every sort are at least three times as common in animals as in man. The art of cooking and the fastidious palate fostered by it, protect us from twice as many dangers as they lead us into.

Several of these poisonings are so wide-spread and so characteristic as to have been given distinct names, such as the "Lupinosis" of the sheep, an acute and extremely fatal yellow atrophy of the liver, caused by eating stacked lupins (plants of the Leguminosæ, or Clover-Vetch family) which have developed poisonous properties, probably from the attack of a micro-organism. The disease will sometimes sweep through an entire province, carrying off thousands of sheep, and has a mortality rate of from 50 to 75 per cent.

Another member of the same family, Crotalaria, or "Rattle-box" lupin, causes the strange "Loco," or delusional insanity, of horses, followed by paralysis, occurring on the Plains of Western North America.

In the large intestine, we have a totally different state of affairs. Here the change has been one of enlargement and a peculiar form of sacculation, not for the purpose of extracting nutritive material from the food contents—for its power in this respect is, of course, extremely limited,—but mainly for the purpose of extracting the liquid portions of the mass in order to prevent too great loss of fluid from the body. This would at least suggest itself as an explanation why the large intestine does not develop until after aquatic habits have been abandoned, and of its consequent late appearance in the ancestral family tree. Now, the commonest disturbance to which this part of the alimentary canal is liable, is an excessive and exaggerated delay and hardening of the fæces in its interior, which results in that probably most common of all morbid conditions, constipation. Here, again, we have a pathologic condition which is simply an excess of a normal one.

Constipation, with all the toxæmic symptoms which follow in its train, is simply an excessive performance of the normal draining and drying function of the colon. One of the forms which occurs in infants (first described and explained by Jacobi) is peculiarly interesting, inasmuch as it appears to be due solely to the late appearance of this part of the gut, of which we have already spoken, which results in its not having assumed the proper arched position in the abdomen at the time of birth. Instead of making a complete arch around the borders of the abdominal cavity, it lies in folds obliquely across it, and hence is liable to obstruction at the acute angles which easily occur in its course. Children otherwise perfectly healthy may have great difficulty in securing anything like a regular movement of the bowels, simply on account of this mechanically disadvantageous position of the gut. But if a little assistance is given by unirritating enemas, and laxatives are carefully avoided, the process of development continues, the gut is pulled up into the proper adult position, and the constipation totally disappears in from one to five months' time.

It is also an interesting coincidence that it is in this same region, which was last in becoming permanently "anchored" by the peritoneum, that, according to Glenard, most cases of enteroptosis first begin, viz., in the right transverse meso-colon, the next to suffer being the enormously distended and twisted folds of the meso-gaster, the phreno-gastro-hepatic omenta.

The diseases of this part of the canal in carnivora and in mixed feeders are much the same as in our own species, but are profoundly modified in the herbivora, as in the case of the stomach, by the great development which has taken place in it. The large gut is the seat of the great majority of violent "colics" to which horses and cattle are so liable. The importance of these may be judged from the fact that they constitute 40 per cent. of all cases of disease in the horse and cause 10 to 20 per cent. of his entire mortality. Of course, the causes of colic are legion, for the name has been indiscriminately applied to almost every form of acute enteritis accompanied by severe pain and distension, its only unity lying in the fact that the huge colon and cæcum (in which 70 per cent. of all cases occur), of a capacity more than ten times that of the stomach, are peculiarly liable to severe and rapidly fatal attacks of tympanites, similar to those already described in the stomach of the ox, and for the same reason. Death occurs in precisely the same manner, by asphyxia, apoplexy, or rupture of both gut and diaphragm.

One of its commonest causes is a unique and distinctly curious one. This is multiple aneurysms of the superior colic artery. These are caused by knots of *Strongyle* worms, which find their way into the muscular coat of the mesenteric arteries and multiply there, until masses are formed large enough to obstruct the lumen of the vessel, or to cause an abscess of its wall which ruptures into it, and thus forms a thin-walled, saccular aneurysm. These verminous aneurysms are extraordinarily common in the horse, Bruckmüller, Ellenberger and others having found them present in from 80 to 90 per cent. of all post-mortems and dissections, so that it is only in a small percentage of instances that they become pathogenic, or give rise to any symptoms whatever during life. Usually they are small and multiple, but they may attain the size of a man's head, and a length of twelve inches, and seem peculiarly prone to excessive development upon the vessels supplying the cæcal end of the colon, although they may be present upon all the branches of the abdominal aorta.

Indeed, Strongyles and other Filariæ seem to be almost normal inhabitants of the blood of the horse and also of the dog, in both of which they occasionally give rise to aneurysms, perforating endarteritis, and even rupture of the heart-wall from an enormous accumulation of them in the cavity of the ventricle in dogs. I found a striking illustration of the second of these, at the Gardens, in a *Dhole,* or Indian wild-dog, (the immortal "Red Dog" of "Jungle-Book" fame), who died of hemorrhage into the mediastinum, from a perforating ulcer of the descending aorta, caused by filariæ.

The same view must almost be taken of the innumerable Flat-worms, Round-worms and Flukes which infest the entire alimentary canal of all species of the lower animals. There are between 70 and 80 species of these, all told, in the domestic animals and poultry alone, and as nearly every species of family of animals and birds yet studied by the helminthologist possesses from one to three intestinal parasites peculiar to itself, the hopelessness of even a complete enumeration of them is obvious. Fortunately it is almost equally unnecessary from a practical or pathological point of view, for although it is a matter of scientific interest to know that there are no less than 34 Tæniæ, 9 Ascarides, 11 Strongyles, and 18 Trematodes or Flukes inhabiting the intestines of the domestic animals and poultry, yet when we find, as every post-mortem room will show, that they are present in from 50 to 90 per cent. of all bodies, and give rise to discoverable lesions in scarcely 1 per cent., it is obvious that the mere presence of parasites is of relatively little importance from an etiological standpoint. In my autopsies at the

Zoological Gardens, I have found one or more species of intestinal worms in two-thirds of the animals, including reptiles, in which careful search was made for them, and yet only in three cases did they give rise to any distinctly pathological condition. In two of these hydatid cysts had undergone degenerative changes and ruptured, one, in a Lemur, into the peritoneum, the other, in a Kangaroo, into the pleural cavity, seriously compressing the lung. In the third, a monkey, a mass of thread-worms (one of which measured 13½ inches in length) had escaped through a duodenal perforation into the peritoneal cavity; though even here they had scarcely set up an appreciable reaction. In the great majority of the numerous hydatid cysts discovered in both liver and lungs, scarcely a trace of inflammation or atrophy, was to be found in their neighbourhood. Most of them were enclosed in a dense envelope of fibrous, often calcareous tissue, and the affected organ had apparently completely adjusted itself to their presence. As to what the relation between these habitual lodgers and their host may be, we are quite in the dark. The advantage is probably chiefly on the side of the intruders, but there is nothing necessarily hostile about them, and they give us a needed warning against the fallacy that the mere presence of foreign organisms, whether animal or vegetable, is sufficient in itself to cause or account for disease. Indeed, we are beginning to suspect that many cases of "parasitism" and "invasion" are really examples of *symbiosis,* in which the relation is mutually beneficial.

Appendicitis.

We have thus seen, that throughout almost the entire length of the canal, the relations between function and structure are tolerably direct and point in a fairly uniform manner in the direction of the principal disease tendencies. There is, however, one extremely interesting region where no such connection can apparently be traced between function and structure, and yet which is of great importance as a site of disease. I refer to the cæco-appendix, which has attained such a bad eminence in pathological circles during the last ten or fifteen years. At this point the connection between structure and function appears to break down entirely, for the simple reason that we can hardly conceive of any useful function which is performed by such a curious and irrational modification of the tube. Here, however, is an illustration of the advantages of the comparative and ancestral method; for as soon as we compare the singular state of affairs in the human species with the various developments of this region in the other mammalia, the problem is at least set in a fair way toward solution. That the problem is one of the highest practical importance and interest, will be readily admitted when we remember that recent authorities upon medicine—as, for instance, Osler and Strümpell—declare appendicitis to be the most frequent inflammatory condition found in the abdominal cavity under thirty years of age, and the commonest cause of peritonitis in males.

The first thing that strikes us about the cæcum is its extraordinary variability in different species. It appears even to excel the stomach in this respect, and upon careful study is found in most cases to be governed in its development by very much the same principles as the latter organ. In its degenerate human form it seems incapable of any useful function, but when we discover it, as in some of the marsupials and herbivorous rodents, reaching a length treble that of the entire body (*Koala*) or a capacity nearly equal to that of the rest of the alimentary canal, we begin to see that after all it is another of Nature's numerous methods of increasing the amount of internal surface for digestive or absorptive purposes. Its variation, according to the nature of the food, is not as direct and uniform as is that of the stomach, and, as Flower has pointed out, it appears to undergo development in inverse ratio to that of the other organ. That is to say, it will appear as if nature increased the absorptive surface of the canal by either distending the stomach or by dilating and elongating a blind pouch toward the lower part of the canal. In the hare family, for instance, in which, though herbivora, the stomach is small and simple, the cæcum reaches a perfectly enormous development, more in capacity than in length.

In most of the Ungulate Herbivora, the cæcum, though large in calibre and well-rounded, and with none of those "stigmata of degeneration" which are so characteristic of the human form, is, compared with the rest of the tract, an insignificant part of the food tube. In the horse, however, the reverse relation has been developed, and the cæcum is an enormous sac having two and one-half times the capacity of the small and simple stomach (Chauveau). In the Carnivora, many Rodents, and the Bats, it is in the majority of species small and imperfect in its development, while in most of the Bears, Badgers, etc., it is entirely absent. Here, of course, it is simply in keeping with the general directness and simplicity of the entire food tube, and it might perhaps be questioned whether this did not represent the primitive type of the organ, of which the intermediate human and anthropoid stages and the extreme herbivorous ones were a later and fuller development. But from the fact that the cæcum is long and well developed in several of the vertebrate groups below the mammalia, double in birds, single in reptiles, is especially well marked and even partially double in the marsupials, and generally better developed in the more primitive members of each of the great mammalian orders than in the more highly specialized forms, unless, of course, these be herbivorous in their habits, the general opinion among morphologists is that the carnivorous cæcum is to be regarded as an extremely reduced form of a somewhat fuller ancestral type. The same general rule holds among birds, the double cæca being both long and full in the lower orders (Ostriches, Waterfowl), small in the higher (Singing-Birds), or absent, as in some Parrots, short in the carnivorous birds of prey, long in the grain-eating Pheasants and domestic fowls.

Indeed, as has been shown by my colleague Dr. A. C. Kerr (to whose kindness I am greatly indebted in my study of this problem, he having placed his collection of over five hundred mammalian and avian cæca at my disposal), in the dog alone many stages of its recession can be seen, even including in one case the development of an apparent appendix. Although the only species which possess a distinct "appendix" (the abruptly-shrunken distal two-thirds of the original cæcum) are the wombat, some rodents, the anthropoid apes, and man.

Now, how does the actual embryonic development of this region in the human species correspond with its general mammalian history? At the earliest appearance of the cæcum during fœtal life, we find it to be a well-developed, tubular prolongation from the gut, of nearly four times its relative length in the adult (proportion to colon, 1 : 5; at birth, 1 : 10; at twenty years, 1 : 20), and of equal calibre with the rest of the gut to its extreme tip. As growth proceeds, however, this relation rapidly changes. The distal two-thirds of the diverticulum is arrested in its development, or even atrophies somewhat, and at about the sixth month the cæco-appendix has become reduced to a structure of the shape of an old-fashioned tobacco pipe, the stem of which represents the appendix and the bowl the cæcum. From this point the disproportion between the two parts steadily increases, the anterior aspect of the "pipe bowl" bulges downward and outward, pushing the stem upward and backward, until finally the appendix, instead of being directly continuous with the lumen of the cæcum, comes to occupy its well known adult position at the upper and inner aspect of its posterior wall. That it was originally a direct continuation of the larger cavity is shown even in adult life by the fact that each one of the three longitudinal muscular bands can be traced directly back to the base of the appendix, and this fact is used as a practical guide to the appendix by surgeons in operating upon it.

The adult relation is attained at birth or shortly after, but the process does not stop here. Since our attention has been called to it by our surgical brethren, careful investigations of the condition of the appendix have been made by Ribbert and others, in the dissecting-room and upon the post-mortem table, with the extremely interesting result of finding that the atrophy actually continues to such a degree that the canal of the process becomes either partially or totally closed in something like twenty-five per cent. of all cases before the thirty-fifth year, while after the fortieth year this percentage rises rapidly until, by the age of forty-five, it is found to be occluded in fifty per cent. And these age-changes, of course, closely correspond with the age-liability to appendicitis and its rapid diminution after forty years of age.

As to the cause of the much greater liability of the male sex to this disease (only twenty per cent. of the cases so far reported being in women), we are still in the dark. One developmental factor only appears to be present, in the fact that the appendix in the female receives an additional artery from the ovarian and hence is better nourished. Many cases of this disease in the female are, however, undoubtedly overlooked and their consequences attributed to perimetritis or salpingitis, and the number of reported cases in this sex is rapidly rising. Paul Mundé thinks it will ultimately be found almost as frequent as in the male. The shorter and smaller the appendix, the larger is found to be the proportion of occlusion.

What suggestions, then, may we gather from this review of the history of the appendix as to its probable disease liabilities? The conclusion, I think, is almost irresistible that we have in the human appendix a structure which is not only ancestrally degenerate, intermediate, as it were, between the voluminous and well-nourished cæcum of our more herbivorous ancestors and the safe simplicity of the carnivorous cæcum, but is also actually undergoing further atrophy during the lifetime of the individual both before and after birth; and we should expect, therefore, upon morphological grounds, to find it a point of least resistance in the food-tube and a frequent starting-point of inflammatory disturbances of every description. And such, of course, is its well-known surgical and medical history. There is no need to call in the aid of foreign bodies or concretions of any sort, fæcal or otherwise.

Any inflammation which sweeps along the food-tube may find in the appendix the tinder which alone is needed for its spark to set up a general conflagration. Indeed, an attack of appendicitis is simply a fulminating exaggeration of the normal process of occlusion and atrophy. Morton has reported two cases of appendices removed, in which virulent colon-bacilli were found "trapped" in the distal part of their lumen, occlusion having first occurred near the base, and I have in my collection an appendix, removed for relapsing appendicitis (three attacks), which was firmly occluded for half an inch from its juncture with the cæcum. The mucous membrane of the isolated, distal cul-de-sac was severely inflamed and showed a patch of gangrenous ulceration. We are beginning to discover that not only in acute infections is this weakness manifested, but that also in protracted septic and other febrile disturbances, attended by great lowering of the general nutrition, the appendix becomes the seat of gangrene, as that point of the abdominal cavity whose nutrition is least thoroughly kept up. A number of such cases have been reported already in typhoid, and many deaths attributed to perforation of the ileum in this disease have unquestionably been due to this cause.

This view of the ancestral nature of appendicitis appears to be sustained by such data as can be gathered from comparative medicine. In cattle, where the appendix or, more correctly, the cæcum, although not relatively large, is still well developed and well nourished, this disease is almost unknown, although it may be the site of inflammation caused by the formation of calcareous concretions (enteroliths); and the same appears to be true of the large and well-developed cæcum of the hare family. In fact, in those classes where it is still well-developed and comparatively functional it appears to be nearly free from disease, except in the horse, as already noted, in whom its huge functional over-development has proved a source of danger from acute distensions. In the Carnivora, on the other hand, the case is the same, but for an opposite reason. Here not only has the distal or appendix part completely disappeared, but even the cæcal pouch is shrunken to a small recess at the junction of the small and large intestine. In fact, it might almost be described in some forms as simply the scar left by the occlusion of the pouch, and even this has disappeared in the Ursidæ, so that it is almost impossible to say where the ileum ends and the colon begins. Even this small recess is occasionally a site of irritation in lions and tigers kept in captivity, apparently from the lodging of bones and other irritating materials in this angle of the tube, setting up a perityphlitis, which, however, is seldom fatal.

In the main, however, the records of canine and feline medicine generally would support the statement that the carnivora are almost exempt from inflammations of this region, on account of the completeness with which they have succeeded in getting rid of the troublesome pouch; and it is, we think, evident that a process tending in this direction is going on in our own species, and although its progress is unfortunately attended by numerous casualties, yet there is hope for the future.

In short, man is the only animal that seems to suffer from appendicitis. In some 400 autopsies at the Zoological Gardens I have never yet succeeded in finding any lesion of the cæcum which it did not share with the rest of the canal, *e. g.*, tuberculous ulceration, which frequently attacks it in monkeys and also in birds. Even the well-marked appendix of the higher apes was perfectly normal in ten specimens examined by Sutton and five by myself but, of course, nothing can be concluded from such a small number of autopsies, especially as very few of these apes live to be even half grown in captivity.

In conclusion, I should like briefly to call your attention to one other disease of the tube whose location appears to me to suggest some connection with its developmental history. I refer to carcinoma. If we were to select five points in the food-tube which were either individually or ancestrally the sites of the greatest variations in development, whose vital balance was, so to speak, the least stable of any parts of the alimentary canal, we should designate as such the pylorus, the cæco-appendix, the œsophagus, and the oral and anal orifices of the tube.

In the first-mentioned region we have not only the point of transition from the secretive epithelium of the stomach to the absorptive epithelium of the intestine, but also a well-developed sphincter and the traces of a second gastric chamber, the so-called *antrum pylori*, which are often well marked in the human stomach. The variations in the shape of the *pars pylorica* are quite considerable, and when we remember that the stomach-region was the site of the "gastric mill" of our crustacean and insect predecessors, of which our pyloric valve is probably a degenerate descendant, and that this area of it has undergone such tremendous specialization in the well-known gizzard of birds, as also in the "grinding-stomach" of several Edentates (armadillo, ant-eater), we can see why it is to be regarded as one of well-marked ancestral instability. The status of the ileo-cæcal region we have already discussed, nor is this limited to the cæcum proper, for the entire colon is a neomorph, and the formative disturbance probably extended some little distance up what is now the ileum.

In the case of the lips and the rectum we have a membrane which has been changed from a cutaneous to a mucous at a comparatively recent period (*stomodæum*, *proctodæum*), and in the former situation, it is the dividing line between the two classes of cells which appears to be a point of attack, a veritable border-land or frontier where, to use a figure of speech, the "thin red line" of cells seem to be in doubt whether they are going to form cutaneous epithelium and produce hair- and sweat-glands or become moist and translucent and produce mucin and mucous glands. Like every border-land, it is a frequent site of disturbances, and particularly of that "rebellion of the cells" called cancer.

In the œsophagus we have the site of those frequently-occurring dilatations, known as crops, which are present in so many of the lower forms of life, and even in some of the higher mammalia, we find this part of the canal singularly liable to form pouches and undergo distension and impaction with dry and irritating food materials, as in the horse, for instance. These pouch-like distensions, known to veterinarians as "*jabots*," becoming filled with chaff or meal, will cause serious trouble from their pressure upon the windpipe, the carotids, and will even encroach upon the lumen of the gullet itself, so that they have to be emptied by vigorous external manipulation, or, failing this, by surgical incision.

Now, if we were to draw up a list of the parts of the food tube most liable to cancerous growth, we should find ourselves confronted with precisely the same regions which have attracted our attention as sites of special ancestral instability. The frequency of cancer is in almost direct relation to the degree of this variability, except in the case of the appendix, whose instability manifests itself otherwise. The most profoundly unstable part of the tube is the pyloric region, and this stands far at the head of all the others in the frequency of cancerous processes, various authors estimating that from twenty-one to forty-five per cent. of all cases of cancer attacking the canal occur at this point. And the same is true in animals, the pylorus being one of the commonest sites of cancer. Next in order of instability, although this is perhaps more individual than ancestral, would come the lips and rectum; and these, again, will stand at the head of the remaining parts of the canal in their liability to carcinomatous change, and last of all the œsophagus. These, of course, may be nothing more than accidental coincidences, but the parallelism is curiously close; and when we further add the facts of the tremendous liability of the pyloric region of the stomach to ulcerative processes, nearly forty per cent. of all gastric ulcers occurring in its comparatively limited area, and the similar susceptibility of the ileo-cæcal region to the perforating ulcers of typhoid (Finney reports that eighty per cent. of all cases are found within ten inches of the ileo-cæcal valve, almost within reach of the tip of the appendix), the suggestion becomes a strong one—that there is some sort of connection between biologic instability and pathologic susceptibility.

CHAPTER IV.

Diseases of the Lungs in the various Classes, and their Morphological Basis.

One of the first things which strikes us in approaching this subject is the high rank occupied by diseases of the lungs as a cause of death.

In the first place we have from 13 per cent. to 19 per cent. of the entire number of deaths in any mortality bills due to pulmonary tuberculosis; and the next most prominent feature in the list will be found to be the so-called "inflammatory" diseases of the organs, as pneumonia, bronchitis, influenza, etc. In fact, by adding together the various forms of diseases of the lung, which appear in the death records, in the human species, it will be found that they are responsible for at least 25 per cent., and, according to some observers, 30 to 33 per cent. of the entire mortality. I do not quote figures, simply because these facts are matters of general knowledge, or if not can be verified in fifteen minutes by any who will take the trouble to turn to the mortality records of any of our large cities or states. Nor is this state of affairs confined to the human kingdom. Definite statistics as to the actual mortality from any cause are of course practically impossible of attainment from our near cousins, the domesticated animals, for the reason that, first, no systematic record of deaths is kept; and, second, that so comparatively few of them, outside of horses, die from natural causes; but such records as we possess seem to point to an almost precisely similar pulmonary mortality in them. For example, such diseases as pleuro-pneumonia in cattle, epizoötic in horses, tuberculosis in horned cattle and in birds, and one of the most fatal forms of hog cholera, are all of them of this nature. Of tuberculosis alone we possess some sort of record, and it ranges, according to the observer, from an average of 15 per cent. to 25 per cent. in the French and English dairy cattle, to as high as the almost incredible proportion of 50 per cent. in the Holstein-Frisians. That is to say, of cattle used in the dairy, anywhere from 25 to 70 per cent. (Haarstick) are said to contract pulmonary tuberculosis at some time during their lives.

There are at least six other great organs or systems of tissues—the heart, liver, food-canal, kidneys with spleen, nervous system, muscles and bones—which are practically of equal vital rank and importance with the lung, among which the remaining mortality is to be divided after deducting quite a considerable per cent. for general diseases, accidents, etc., which are not to be classed as belonging to or focalizing in any particular organ or system. Diseases of the entire alimentary canal and its appendages, for instance, which might justly be divided into three separate regions of almost the extent and importance of the lung, including typhoid and cholera, are responsible for barely 10 per cent. of the mortality in the human species, and cardiac mischief is responsible in most vital statistics for scarcely 5 per cent. So that the part played by the lung in bills of mortality is really far out of all proportion to its actual vital importance.

The causation, course and general character of disease of the lung are practically identical in all mammals. This was of course to be expected, so far as anatomical grounds are concerned, as almost the only changes undergone by the organ in the entire class are those of lobation and relative volume. Chills, infections, zymosis, inhalation of dust, foul air, etc., are the principal causative factors, just as in our own species.

Pulmonary disease appears to be distinctly more frequent in animals that are stabled or housed, such as horses, dogs, and dairy cattle, as compared with range horses and cattle, sheep or goats. The acute disturbances, coryza, influenza, pneumonia, bronchitis, are more common in horses and carnivora than in the herbivora generally, both domestic and wild; but this is more than counterbalanced by the much greater susceptibility of the latter to tuberculosis.

The susceptibility of the lung to disease ranks almost as high as in our own species. Not only, as we have already mentioned, do tuberculosis, epizoötic in horses, influenza, and two of the most fatal forms of swine plague or "hog cholera," kill by the lungs; but glanders in the horse has the same proclivity. The pleuro-pneumonias of cattle, the contagious pneumonias of the horse and dog, the verminous bronchitis of sheep, play as fatal a rôle as our own pnemonia and bronchitis. Law specially comments upon this fatality, and quotes as an illustration Percival's report of ten years attendance upon the horses of the 1st Life Guards. Of 667 cases of serious illness in this period, 300 were diseases of the lung; and of seventy-seven deaths, excluding those by glanders or accidents, fifty-seven were due to pulmonary disease.

In most wild animals in captivity the same condition of affairs exists. In seventy autopsies upon monkeys and apes at the London Gardens during the past nine months, the apparently fatal lesions were found in the lungs in nearly 70 per cent. Other observers have found as high as 80 per cent. of the death-rate in monkeys due to pulmonary mischief. Of twenty-two marsupials examined, seventeen died of lung disease, twelve by septic pneumonia in the course of a curious infection, beginning with gangrenous ulceration about the roots of the incisor teeth. Among seventeen carnivora, in which a reasonably clear cause of death was found—nearly half of this order examined presenting no discoverable lesions whatever *post-mortem*—the lungs were its site in seven, or 40 per cent.

So that the lung would appear to be, for some reason, a point of least resistance in both man and animals. Suggestions as to the probable reasons of this susceptibility will be discussed later.

In birds, however, we find a widely different state of affairs. Instead of the lung being the most frequent site of fatal disease among the great organs it is one of the least so. Out of sixty-two necropsies upon birds, in which a reasonably clear anatomical cause of death could be discovered, at the Zoological Gardens, in only fourteen was this situated in the lungs. The liver, the alimentary canal, the air-sacs, were all more frequent sites of serious lesions, and even the heart fell only a little way behind the lungs. And these deaths were chiefly due to pneumonia, bronchitis, "gapes" (worms), and mould invasions, for, as will be seen in the chapters upon tuberculosis, the onslaught of this great death factor in birds falls chiefly upon the abdominal viscera, only attacking the lungs at all in about one-sixth of the cases.

This coincides with such veterinary records as we possess, for the most part, unfortunately, few and imperfect, of the incidence of pulmonary disease in birds.

There exists no great epidemic disease in poultry chiefly attacking the respiratory organs, although these are the third commonest site of fatal lesions in the well-known "chicken cholera," or "hen typhoid."

The nearest approach to this is the widely spread "gapes," due to a Strongyle worm which affects a lodgment in the nasal cavities, pharynx and upper part of the trachea, in which last situation, generally just below the glottis, it causes death by mechanical obstruction of the air passage, or laryngeal spasm. The lung parenchyma is seldom attacked or even affected, except by congestion due to suffocation, and the fatal effects of the disease closely resemble those of laryngeal diphtheria in our own species.

An invasion of the trachea, bronchi, and abdominal air-sacs connected with the latter, by acari *(Cytodytes)* also occurs, but again the lung parenchyma escapes in a curious manner, except as a result of obstruction of the air tube supplying a given area of it.

I have found the "gapes" Strongyle a cause of death five times in the sixty-two autopsies referred to, chiefly in water-fowl (swans), although it used to be extremely fatal among the pheasants until stringent precautions were adopted to secure the drinking-water from contamination, and to either change or thoroughly disinfect the soil of any run in which the disease had occurred. The tracheal irritation in all these was intense, and the worms were found in some cases scattered the whole length of the "French-horn" trachea, which in the swan bends and returns upon itself in a most complicated manner, but more commonly collected in groups or even knots at the bends of the tube, or in the neighbourhood of the syrinx.

As to the cause of this lower susceptibility of the bird lung we are quite in the dark, although it presents several anatomical peculiarities which may have some bearing upon the question.

In the first place, the bird lung is smaller,—little more than half the relative weight—firmer, more vascular, and less expansile than the mammalian organ. The last of these conditions would diminish the extent of its exposure to aërial infection, and its smaller size and greater vascularity would probably increase its resisting power as a tissue.

In the second place, the more we study the structure of the bird, especially from a pathological point of view, the more we are driven to the conclusion that a most important, if not indeed the chief part in its respiratory activities, is played by the elaborate system of huge air-sacs into which the bronchi are continued. These are from seven to nine in number and occupy the entire body cavity, from the clavicles to the pelvis, and at their outer borders open into the medullary cavities of a varying number of the bones. Developmentally, they are simply immensely expanded pulmonary alveoli, continuations of the lining membrane of the bronchi greatly attenuated. And while at one time regarded as exclusively for the purpose of "lightening" the body for flight, morphologists are more and more coming to regard them as chiefly respiratory in function. Which position is strengthened by the curious analogy that exists between them and the numerous tracheæ and air pouches, opening all over the body surface, in those "Invertebrate Birds," the Insects.

If we are justified in regarding these as part of the respiratory system, then a large part of the discrepancy between the frequency of respiratory diseases in birds and in animals is accounted for at once. Although in my sixty-two necropsies, only fourteen deaths were due to lung lesions, no less than fifteen were due to changes in the air-sacs, making a total of 29, or 46 per cent., which practically reaches the mammalian average.

These lesions were of a unique character, and consisted in the great majority of cases (twelve) of an invasion by mould-growths, principally *Aspergillus*. From one to four sacs were usually affected, and their involvement varied from three or four rounded and cupped masses of growth of the size of a shilling, upon the inner surface of the sacs to a complete coating or lining, in some cases filling up the entire lumen of the cavity. The mould-growths seemed to provoke the out-pouring of a firm, cheesy exudate, which usually formed a plaque-like layer underneath them from a sixth to half an inch in thickness, and could be shelled out of the cavity, forming a more or less complete mould of the sac. In two cases this exudate, of the consistency of cream-cheese, filled and distended the entire sac, in one of them, a Bateleur eagle, to the size of a lemon.

In most cases the free surface of these plaques, often of a curiously cupped or nest-like shape, was covered with a profuse "fur" of green, brown, black, or occasionally white mould, scrapings of which, under a low power, showed abundant mycelium and cone-shaped or drumstick-shaped spore masses.

The cause of death in most cases was a general cachexia, due apparently to the absorption of toxic substances from the mould-plaques, but in three of them, the eagle referred to, a duck and a swan, death was produced by the lodgment of a plaque-colony in the trachea, forming a close-fitting plug, which absolutely blocked its lumen, and in one case showed, when removed, a perfect cast of the bifurcation and beginnings of the bronchi.

The lungs were invaded in a few cases, but never to any important extent, a few lentil-shaped nodes upon the surface of the organ being the greatest involvement. In four cases, all in water-fowl, in which abundance of mycelium was found in the air-sac plaques, repeated examination of the pulmonary nodes by Dr. Foulerton failed to discover any trace of mycelium whatever.

These aspergilloses of the air-sacs, trachea and lungs are well-known in poultry and house birds, where they have been fully studied and described by Boyce, Generali, Dieulafoy, Vidal and others. They are referred to *Aspergillus glaucus*, *A. nigrescens*, *A. fumigatus*, and *Mucor racemosus*. Death is described as due to emaciation and diarrhœa, the disease running its course in a few weeks.

The incidence, symptoms and causation of respiratory diseases in mammals, are so similar to those in our own species, that little more than a recapitulation of them is necessary.

Coryza and *influenza*, under which latter name are probably grouped together, as in our own species, various epidemic forms of catarrhal affections of the upper parts of the respiratory passages, are quite common in dogs and horses, but rarer in cattle, sheep and pigs.

The commonest form of the celebrated "Epizooty," "Epizootic," "distemper," "pink-eye" of the horse is an influenza of severe type. Like its counterpart in the human species it spreads with great rapidity, and though varying greatly in severity in different epidemics, usually assumes one of the three great types recognized in our own species, the pulmonary or pneumonic, the gastro-intestinal and the nervous, according as the violence of its attack falls chiefly upon each of these great systems. So deeply does its preference color the type of the disease, that its various manifestations have been classed as separate diseases.

Especially in the case of the gastro-intestinal form, which has been termed "typhoid of the horse," on account of the congestion of Peyer's patches found in it. Serious cerebral symptoms and paralysis may follow the nervous form, and death by cardiac failure is not uncommon. Generally speaking, however, its mortality is low (1 per cent. to 4 per cent.), and in this, as well as the rapidity of its spread and violence of its onset, it keeps closely parallel with the human type of the disease.

It has been alleged by various authorities that epizootic in the horse and other domestic animals usually precedes an epidemic of human influenza, but this has certainly not been the case in some of the largest epidemics, and while cases of alleged transmission of the disease to grooms and stablemen have been reported, these have usually been found to be glanders, and the connection between the two epidemics is quite doubtful.

The disease is quite common in dogs, and sometimes assumes very severe forms. An epidemic of it was raging among the dogs of Western Europe, England, and Scotland early in the present year, characterized by a curious gangrenous inflammation of the gums and lips, rapidly extending to the other mucous membranes, and not infrequently proving fatal.

Among sheep and oxen the disease is rare, and usually of a mild type; and the same is the case in poultry, where it forms one of the group of nasal catarrhs known as "the pip."

The nasal cavities and accessory sinuses of sheep are, however, subject to invasion by the larva of a fly (*Œstrus ovis*), which produces an acute nasal and lachrymal congestion, followed by severe cerebral symptoms, as the larvæ work their way into the frontal, sphenoidal, and ethmoidal sinuses, and even penetrate the cranial cavity through the cribriform plate. The patients have attacks of vertigo, and an irregular gait, which closely resembles that of "turn-sickness" or "gid"—a much more serious and fatal cerebral disease, due to the lodgement in the brain of the cystic form of a tænia (*T. Cœnurus*). These symptoms have given the disease its name of "false turn-sickness."

Laryngitis, both acute and chronic, is fairly common in horses, especially those which are kept in warm stables or fed upon mouldy hay, but rare in cattle, sheep, pigs, and dogs.

A curious and unique laryngeal affection occurs in horses. This is the familiar *roaring* or *wheezing*, due to paralysis of the muscles supplied by the recurrent laryngeal nerve, chiefly the posterior crico-arytenoids. As these are dilators of the glottis, the cords cannot be widely separated in rapid respiration, and hence their slackened borders and even the arytenoids themselves are sucked into the glottis at each inspiration, producing the roaring sound which has given the disease its name.

It is quite common among racehorses and English thoroughbreds, and frequently runs in families, especially upon the male side — a third of the colts of affected stallions are said to become roarers. It is almost always (ninety-six out of 100 cases tabulated by Günther) the *left* recurrent nerve which is affected. The reasons for this, and indeed the cause of the disease itself, have given rise to much controversy, and are still quite undecided. It is, however, generally agreed that the nerve becomes affected in the thoracic part of its course, and pressure by enlarged lymph nodes, aneurisms, œsophageal pouches, pleuritic effusions, etc., have been assigned as causes. As, however, the disease is extremely slow in its course, so that death usually occurs by some intercurrent disease, opportunities for autopsies are not very frequent; and while these conditions have been found in a few cases (Bassy, Fergusson, Esser), yet in others no such appreciable cause can be discovered. In some cases the paresis unquestionably comes as a peripheral neuritis, or neuro-toxis, following chronic lead poisoning, or the curious "lupin poisonings" produced by lupins, clovers, and vetches under certain conditions, especially if mouldy or badly cured.

So that the conclusion appears to be forced upon us that we have to do with a special vulnerability on the part of the recurrent nerve, probably connected with its extraordinarily circuitous and exposed course, due to the "stretching" which it has undergone by reason of the descent of the heart and branchial arches from the pharyngeal region in the embryo to their present position. This is strengthened by the fact that this nerve is the commonest site of paresis in the human larynx. Also, that the left nerve, which is both carried further out of its course and exposed to the throbbing of the aorta, is far more susceptible than the right.

Indeed this aortic throbbing tension has been advanced as the chief cause of the paresis by Ellenburger, Frank, and Martin, all of whom point out that it is in race-horses and other thoroughbreds, who have both to gallop at high speed for considerable distances, and in whom the neck has become unusually long and slender that this disturbance is most likely to occur. A long neck has always been regarded as a predisposing factor.

On the other hand, it is urged that the disease is not infrequent among draught-horses, but it must be remembered that, in any horse, the elongation undergone by the nerve is most considerable, and that this class of animals are habitually called upon to make severe and sustained exertion in pulling, which would produce as violent aortic throbbing and tugging as any gallop. Nocard has recently made one of his brilliant and illuminating reports upon the disease, in which he inclines to the conclusion, avowedly preliminary however, that the paresis is the result of a neuritis following some systemic intoxication or infection, most frequently strangles, the nearest analogue to diphtheria in the horse.

in which case it bears a curious resemblance to our own post-diphtheritic paralysis.

But this of course, like the other systemic poisonings, leaves the left recurrent,—except in the cases in which the paresis is due to direct pressure by enlarged glands,—a point of least resistance in the entire nervous system, whether from its singular course and the tension put upon it, or from yet unknown causes.

It is a curious coincidence that the horse, in whom, of all our domestic animals, the neck has become most elongated, and the heart has the most violent strain put upon it, is practically the only one to suffer from this striking disease. A few cases have been seen in work-oxen and in dogs, but the disease is practically unknown outside of the equine species.

It may, perhaps, appear somewhat improbable that a physiologic and immeasurably gradual elongation of the course of a nerve, taking hundreds of generations to accomplish, however little to its advantage, could be capable of working injury to it, or even lowering its resisting power. But, it is of interest to remember that the only other nerve in our own body, which has been dragged round a morphological pulley, so to speak, in such fashion, the spinal accessory, is singularly liable to those attacks of painful spasm in the muscles it supplies, known as "wry-neck," or torticollis, both constant, after exposure, and spasmodic, or idiopathic. The worst cases of spasmodic torticollis, as Morton has shown, which have defied all other treatment, can be relieved by stretching, and permanently cured by resecting the spinal accessory.

The treatment of roaring is at best only palliative, and the disease usually steadily progresses to a fatal termination in the course of years. It can be "short circuited" by tracheotomy and the insertion of a tube, and so effective is the relief by this device, that it is said that in a field of twenty entered for one of the great stakes, some years ago, no less than five of the starters wore tubes, and one of the "silver-whistlers" won the race.

The annoying roaring, wheezing noise, is sometimes attempted to be prevented in cab-horses by the crude and rather inhuman methods of buckling a strap round the throat, or putting pads over the nostrils. By this means the current of air entering the trachea is diminished to such a degree that the left arytenoid and cord are not sucked into the glottis by it. But these devices, unless their pressure is increased to a cruel degree, are of little effect, and, of course, rather aggravate than relieve the disease.

Complete resection and removal of the affected cord and arytenoid have been practised with good results by Günther and Möller; and recently Tagg* has reported a most ingenious section of the nerve, with suturing of the peripheral end into the trunk of the vagus, in the lower third of the neck; followed by a cure in six months.

The various forms of *bronchitis* and *bronchial catarrh* are found in most animals, but much the most commonly in horses. This seems largely due to the fact that they are both kept in warmer and less open stables, and left standing exposed to the weather after exercise, in a way that no other animal is. It also occurs in hounds that are hunted hard and kept in damp kennels.

The causes are the familiar colds and chills, impure air, dust and smoke in the inspired air, or the extension of nasal catarrhs, influenza, glanders, etc. It is especially common on board overcrowded ships upon long voyages, and a septic form of it is the principal cause of the frightful mortality

* "Journal of Comparative Pathology," 1896, p. 345.

which up to ten or fifteen years ago not infrequently occurred upon our Atlantic cattle ships. And here it attacks cattle and sheep as well, although neither of these species is commonly subject to it on land. Severe storms which compel the battening down of the hatches, or hot calms, or even gentle winds astern, giving no " head breeze " for ventilation purposes, will mow down thirty, forty, and even eighty per cent. of the living cargo by a form of septic bronchitis and pneumonia, similar to that which carried off most of those who survived till morning in the Black Hole of Calcutta.

Usually, however, the course of the disease is mild, even when following an infection, although it not infrequently assumes the capillary form and gives rise to alarming symptoms.

One form of the disease is unique in its causation, and that is the "*verminous bronchitis*," or " worm tuberculosis " of sheep, and occasionally of oxen and young pigs. This is due to a lodgment in the bronchial passages, and ultimately in the lung-parenchyma, of the eggs, embryos and adult forms of a strongyle worm. In the lung tissue these form small nodules, closely resembling at first sight tubercular foci, but upon examination with a low power, or even a good pocket lens, coils and knots of white, thread-like worms can be made out in their interior.

The symptoms of the disease when severe resemble a chronic bronchitis, gradually deepening into pulmonary tuberculosis. It is, however, usually slight in its effects, and I have found sheep in our slaughter-houses whose intestines and lungs were thickly sprinkled with these " worm-knots," or their calcareous remains, and yet appeared in every other way in prime condition. Among weak flocks, or in a bad season, it may reach a mortality of 30 per cent.

These "*worm-knots*" have been found quite frequently in my necropsies at the London Gardens, but never in sufficient numbers to give rise to any apparent mischief. Indeed, in most cases they seemed to lie in the tissues, simply surrounded by a thin, fibrous envelope, much as an encysted bullet would. In some instances the coils of the tiny white or yellow worm could be made out by close scrutiny with the naked eye. The disease has a wide distribution, as it was found in the lungs of monkeys, of kangaroos, badgers and ichneumons, and in the intestines of sheep, monkeys, a wallaby, and several species of birds.

An acute, infectious, and, considering the slightness of the lesions produced by it, a surprisingly fatal form of *bronchitis* was also very common among all the animals. It usually ran its course in four or five days, and only a slight congestion, with occasional localized œdema or emphysema of one or both lungs, would be found. The bronchial tubes and trachea, however, would be filled with a frothy, blood-stained muco-pus, which often escaped from both mouth and nostrils.

The disease is particularly fatal among the anthropoid apes, as of the five specimens which came under my observation, no less than four died of it.

It is the third commonest cause of death in monkeys, and divides with pneumonia the heavy pulmonary death-rate of the carnivora.

Pneumonia is also as widely spread among animals as in ourselves, and from almost identical causes. Infection, most frequently by a micrococcus, *Diplococcus pneumoniæ equina* (Schütz, Cadeac), chills, gases, or dust in air, especially from mouldy hay, are among the most frequent.

There is a well-marked croupous form in the horse, more rarely in the ox and the dog, which runs through the well-known stages of red hepatization, grey hepatization, crisis and recovery by resolution, its mortality being quite moderate. Then we find simple catarrhal pneumonias after chills or exposure, pneumonia following influenza, and that due to the extension of bronchitis.

One form, however, has no representative in our own nosology, and that is the dreaded epidemic, *Pleuro-Pneumonia*, *Contagious Pneumonia* of cattle; after cattle-plague, the most fatal disease of the bovine species. In Great Britain 200,000 cattle died in 1860, and in six years, over a million, by this scourge. Lately, however, its ravages have been greatly diminished by vigorous quarantine and preventive measures. As a rule it kills or disables from 50 per cent. to 70 per cent. of the animals attacked. Its symptoms might be roughly described as those of a bubonic plague of the lungs and pleura, though it runs a much slower course. It is unquestionably of bacterial origin, but the precise form concerned does not seem to have been satisfactorily identified as yet, although there are many claimants for the honour, notably the *Pneumo-bacillus liquefaciens* of Arloing, Zuill, and Lustig.

Pleurisy is not infrequent in dogs and horses, differing from the human form chiefly in the fact that it is rarely of tubercular origin, both these animals being almost immune to tubercle, and that enormous fibroid thickening (2 to 3 c.m.) of the membrane may develop. Although it occurs frequently as a result of chill, exposure or injury, it is regarded as usually of bacillary origin, the chill or injury having lowered the resisting power of the pleura, as it does that of the lung in pneumonia. The exudate may be serous, purulent, pseudo-membranous or plastic, and although the primary form of the disease is not infectious, yet exudate drawn from a diseased pleural cavity and injected into the pleural sac of a healthy animal almost invariably sets up an acute pleurisy.

Asthma in animals is almost limited to two species, the dog and the horse. In the former, it is chiefly found in the over-fed, over-housed, under-exercised pet dogs of large cities, especially pugs. The symptoms are ludicrously human, coughing, wheezing, gasping for breath, and the causation is identical. It is regarded as, in most cases, a vasomotor neurosis, at times resembling an urticaria of the bronchial mucous membrane. It may be relieved by antispasmodic and antilithæmic treatment, but is extremely obstinate and chronic in its course. It gives rise frequently to emphysema.

In the horse, asthma resulting in extensive emphysema is one of the chief causes of that well-known symptom-group, covering various morbid conditions, called "*Broken-wind.*"

The feature common to them all is a chronic dyspnœa, worse on exertion, depending upon more or less extensive emphysema of the lungs, and any disease or strain which gives rise to this condition may be a cause of broken wind. Indeed, so wide is the term, that any form of chronic dyspnœa, such as that due to obstruction of the upper air passages by tumors or any other cause, congestion of the lung in valvular mischief (known as "*cardiac* broken wind") and old pulmonary adhesions and fibroses may be included under it; but far the largest proportion of cases is due to emphysema following asthma or other neurosis of the vagus.

These are attributed by Law to a rather curious cause, over-feeding with hay, especially of clover, lucerne, vetches, or lupins. Thus making this widespread condition a toxo-neurosis, if not neuritis. And the distribution of broken wind corresponds singularly closely with that of clover-hay. It is practically unknown in range-horses in either North or South America, in Arabia, Persia, Turkestan, Spain, and Portugal; and in all these countries no clover whatever, and very little hay of any sort, is given to horses. Even in Europe it is generally admitted that no horse ever became broken-winded at pasture. The use of straw in the place of hay will secure an immunity from broken wind, as is illustrated by two districts side by side in France: Segala, where hay is freely used, and broken wind abounds, and Causse, where straw is used, and the disease almost unknown. (Demoussy.) The same has been pointed out in several Spanish provinces by Rodriguez. Roughly speaking, wherever wild or prairie hay is used, in the United States, the disease is almost unknown, while in tame-hay districts it abounds; and large owners of horses who have given up clover-hay, and cut down sharply upon the amounts of hay of any sort used, have almost got rid of the disease in their stables. Thousands upon thousands of tons of baled prairie hay are shipped half across the continent for use in the great stables and breeding farms of the Eastern States, where it brings a high price on account of its superiority to the home, or "tame" product.

This toxic effect of clover-hay is by some ascribed to the moulds and other growths upon it, when badly cured, but there seems no question that even the sweetest and soundest of hay will, if eaten in sufficient quantity, give rise to these and other "thick-winded" symptoms. It is a most curious fact that all the fodder plants of the great Leguminosæ family—lupin, vetch, clover, chick-pea—renowned for the small number of members in it which are poisonous in either seed, leaf, or root, and of priceless value to the farmer, may under certain conditions, when dried, give rise to grave toxic symptoms. One of these is so frequent and serious as to have acquired a name of its own, "Lupinosis," and we are utterly in the dark as to the conditions upon which this change depends, as it is quite independent of mouldiness, fermentation, or bad curing of any sort.

Law regards broken wind as a reflex disturbance of the vagus due to gastro-intestinal mischief, although in some respects it more closely resembles a neuritis due to intestinal toxaemia. In many cases, according to De Moussy, the emphysema is attended by widespread aneurismal dilatation of the capillaries of the lung.

Now, let us look for a moment at the reasons which have been advanced for this high grade of vulnerability upon the part of the lung. First of all it is usually urged that the lung is peculiarly exposed, especially in the changeable climate of the temperate zone, and more readily attacked by changes in the temperature, moisture, and electric tension of the air which must be breathed into it. But we think this exposure theory begins to reveal its weakness, when we discover, first of all, that the proportion of fatal lung disease in any given race or class, particularly of tuberculosis and pneumonia, is in exactly inverse ratio to the amount of exposure to all sorts of climatic vicissitudes to which its members are subjected. Diseases of the lung are emphatically diseases of city dwellers, or of such classes in the rural population, as, for instance, farmers' wives and daughters, who suffer from too little fresh air and sunlight. In cattle the same thing is even more strikingly illustrated. Tuberculosis in particular, and pleuro-pneumonia in a less degree, are emphatically diseases of stabled cattle or cattle of limited range, and except in the virulently infectious forms of the latter are comparatively unknown in range cattle.

Besides, when we come to look at the wonderfully elaborate and effective mechanisms in the nostril sieve and turbinated steam coils which nature has made for both warming and moistening the inspired air, so that, as was shown by Mackenzie, air at even little above the temperature of zero is raised to within two or three degrees of the body temperature by the time it has penetrated to the naso-pharynx, we shall, I think, be able to see on anatomical grounds both the weakness of this exposure theory and the reason why, in its purely mechanical form, it is becoming so universally discredited in clinical etiology. The chilling effect of inspired air upon either nose, trachea, or bronchi is the very least of the factors which result in the production of that most common but positively ludicrously misnamed pathologic process, a "cold," which would much better be termed, if it were not for possible confusion with the language of the turf, a "foul."

But, of course, this may be true as regards mere climatic exposure to perfectly pure air, and yet the case be altogether different with the air which very many of these city-dwellers are compelled to breathe, loaded as it is with emanations from the bodies and lungs of others, dust, sewer gas, and impurities of all sorts and descriptions. This may be granted, and yet we must remember that the wonderfully efficient barring-out mechanism still plays an important part even here, as can be seen by the condition of the nasal mucus after a day spent in a particularly dusty atmosphere, and further that this same course of reasoning would apply with tenfold effect to the stomach under these circumstances. And when we remember the dietetic errors of excess upon the one hand and of deficiency and poverty upon the other, the nauseous slops and messes, the greasy and half-putrefying dishes, sauerkraut, limburger, soda biscuit, "high" game, unleavened bread, and gastric atrocities of all sorts and descriptions, to say nothing of unfiltered water, stale beer, and sour milk, I think we shall have to admit that, on *a priori* grounds, we would expect at least as much fatal rebellion on the part of the stomach as of the lungs. Air in the vilest den is seldom quite so bad as the food.

The next explanation advanced is that of complexity of structure; that we have here an organ of very high grade, as it were, of vital metabolism, and consequently, like all delicate machinery, peculiarly liable to get out of order; but a single glance, I think, is enough for this theory. Important as the function is, the actual process which takes place in the lung itself is one of the simplest and most purely mechanical that can be found anywhere in the body. All that the epithelium has to do, so to speak, is to keep out of the way of the rush of the imprisoned carbon dioxide toward freedom and of the oxygen toward the hæmoglobin. Its sole function is to keep itself alive and pervious.

Then we have the statement made that the lung is almost the only organ in the body which never rests and is obliged to remain in constant activity as long as life lasts. But this is, we think, even more inadequate, for the reason that, upon this principle, the heart ought to have at least as high a morbidity as the lung, instead of having about one-tenth of it; and secondly, that the real, active work of respiration is done entirely by the muscles and nerves of the chest, which are extremely seldom the site of disease. The lung proper is as passive in this respiratory movement as it is in the exchange of gases through its epithelium.

These are the explanations usually advanced, and I think that no one of them alone is, nor indeed are all taken together, in any real sense, satisfactory explanations of the extraordinarily high degree of morbidity of the viscus. As in other problems, when existing conditions do not appear to explain any given phenomenon we are inclined to turn toward the light of history. And here at once, I think, we come upon a distinctive and unvarying characteristic of the lung, as an organ, which marks it off from almost all other organs of the body as abruptly and as positively as does its marked liability to the attack of disease, and that is its extreme recentness. With the exception of the uterus and mammary glands, there is no organ in the body which has not from five to ten times the length of ancestral history that the lung has. Appearing as it does for the first time, and in a morphological sense *de novo*, at the level of the amphibia, with no invertebrate history whatever, and but the merest fragments of history in the longest and largest portion of our vertebrate family tree, it is a thing of yesterday, morphologically considered, as compared with any other of the great organs of the body. The stomach, for instance, goes back to the hydra, or even in an impromptu form to the amœba itself. The brain has a pretty respectable representation from the time of the middle cœlenterates and certainly of the worms. The heart goes back to almost the same point. The kidneys have ancestors in that illustrious predecessor of ours which has been degraded to the base use of concealing fishhooks. The liver itself bears a distinct family likeness to its ancestor in Molluscan times; and so on all through the list of our body organs.

In short, the lung represents an adjustment of the body mechanism to an extremely late and recent factor in our environment—the direct breathing of air. Can this fact of recentness be said to have any pathologic bearing? I think that it can, and that it may almost be laid down as a law, that in pathology as well as in biology the ancestrally old is the individually stable and resisting, and conversely, the ancestrally recent is the individually unstable and vulnerable.

But have not all our organs also been compelled to adjust themselves to this air-breathing state of affairs? We are land animals, and our entire structure has been modified to meet the change. To which I will venture the reply that not only is this not true in equal degree of other organs, but, strictly speaking, no other organ or organs in the body have so adjusted themselves, except in the most superficial manner. We talk about our body republic being an air-breathing and land-living organism, but as a matter of fact all of our citizen cells outside of the lung are still absolutely and necessarily aquatic in their habits, and marine at that; they cannot live except when kept continually bathed in a normal saline solution.

First of all, upon *a priori* grounds, I think we should be justified in the conclusion that the longer a given organ has performed its function in an adequate and satisfactory manner (and this is of course simply what is meant by the remoteness of its appearance in the family tree) the more likely it will be to continue to perform that function, undisturbed by any influences which may be brought to bear upon it. The mere presence and history of such an organ, for instance, as the stomach, are a standing "certificate of good behaviour" for the past fifteen or sixteen millions of years, and like all other such "characters" would be entitled to considerable weight in calculating its probable performances in the present and the future.

And, secondly, I think it will be quite possible to show that those organs or functions which are the last acquired are the first to fail or disappear, either in the normal history of the body or under the stress of adverse circumstances. Take for instance the only other organs of importance, which are more recent than the lung itself—the mammary gland and the uterus. Late in their appearance, not only ancestrally but also individually, as to the establishment of their functions, they are the first organs of the entire body to fail and atrophy; in fact, almost the only ones which normally do so before the appearance of actual senility of the general system. And what is their pathological record? One of the blackest for the length of their existence and their importance to the individual which is to be found in the entire mechanism. Nearly 75 per cent. of carcinoma in the female will be found to have its site in these organs, while it would, I think, be a conservative estimate to say that one-third of all women are, more or less chronically sufferers from some form of pelvic disturbance, even while admitting that much of this may be reflex or but a cloak for our ignorance.

Another case in point is that of the higher cerebral powers, the imagination, the creative faculty, the memory. Appearing for the first time in the higher mammals and at a comparatively late period in the individual, they are among the first to fall before the onslaught of either the febrile or intestinal toxæmias or the general decadence of old age.

The same may be said of our power of locomotion in the erect position. Appearing elsewhere only in our double first cousins, the gorilla and orang-outang, and most difficult of acquisition in our own anthropoid stage, it is one of the first things to disappear under the disabling touch of serious illness or in the development of the tottering and trembling gait of threescore years and ten. The attitude of the white-haired grandsire, tottering along in the autumn sunshine, would be almost ludicrously anthropoid, if it were not so pathetic in its helplessness; and the cane with which his feeble balancing power is reinforced, is a civilized imitation of the broken bough, with the aid of which the gorilla shambles through his native forests. And as Dr. Charles Cary has acutely pointed out, the old man totters *not* from weakness but from loss of balancing power and confidence.

It need hardly be mentioned that in the realm of morals and manners this law is already accepted as a truism, which has been proved time and again, for instance, by the awful excesses of mobs, as during the French revolution, and the frightful disregard for the rights and welfare of others, to say nothing of the decencies and amenities of civilization, which will be shown under the pressure of panic, hunger, or pestilence. The later veneer of civilization scales off like the viper's skin at the slightest touch of stress or danger, and this rapid blunting of all the social graces and matters of minor conscience, which are the last things acquired in the development of the individual, is one of the most constant and striking symptoms of the approach of chronic forms of insanity. Last to bloom and first to fade is as true of the faculties and even of organs as it is of flowers.

If we could speak of the body republic as composed of a confederation of sister states, we should say that the lung was the literal Mexican republic of the entire system—a thing of yesterday by contrast with the stomach or brain, imperfectly adjusted to its new conditions, varying constantly, as I shall attempt to show later, and liable at any time to the outbreak of fatal rebellion or serious insurrection. In short, I believe that nothing less fundamental than some such factor as this, will explain the extraordinarily disproportionate morbidity and mortality of the lung.

Correlated with the recentness of the appearance of the organ, is the fact to which we have already briefly alluded, that it is the farthest departure from the original water-loving and water-living type of the primitive cell. There are no other cells in the body, which really live in or upon air, even though only upon one of their lateral aspects. All the superficial epithelium of the skin-sheet, so long as it retains its vitality, retains its moisture, and by the time it becomes dry it is practically dead and only mechanically adherent to the body, ready to be shed at any moment. It is perfectly at liberty to protect itself through either oil or keratin, while the lung cell must remain readily permeable.

In short, I believe that we have a fair morphologic basis for regarding the lung as a point of least resistance in the entire organism, a weak spot in the line of defence, and this I think will be seen more clearly from the pathologic standpoint, when we come to examine the nature of the majority of the diseases to which it is subject. Head and shoulders above all other processes in these organs, stands the "great white plague of the North," as Oliver Wendell Holmes vividly termed it—tuberculosis. Tremendous as have been the developments of this disease and wide as the differences of opinion may be as to the balance of the factors in its etiology, the soil and the seed, all observers are agreed that its most powerful predisposing factor is lowered resistance in the individual or organ attacked. Of all the deaths which are ascribed to diseases of the lungs in the mortality reports, pulmonary tuberculosis claims from 60 to 75 per cent. Nor, I believe, can this extraordinary liability on the part of the lung be accounted for solely or even chiefly upon the grounds of entry or exposure, for the tubercle bacillus is one of the most ubiquitous organisms which has yet been demonstrated in the human tissues. It is to my mind a significant fact that each point at which it succeeds in effecting a lodgment and establishing a breeding-station, is the point at which there are tissue elements of a low degree of resistance, either from rapid growth and the presence of immature cells, or from the opposite process of atrophy and absorption. Its commonest sites are the lymph nodes, where the blood is in process of manufacture; the growth lines of the bones in young life, where a rapid and tumultuous production is constantly going on; the bodies of the vertebræ and intervertebral discs, where the notochord is even yet in process of absorption. And the points where the notochord longest persists are the regions of the vertebral column where tuberculous caries is most likely to occur. I cannot but regard the singular fatality of the pulmonary form of this disease as due not so much to the respiratory tract being the most common port of entry for the bacilli or their spores, as to the fact that here, and here alone, they find a thoroughly congenial soil in a vital part. To speak metaphorically, once let the tubercle bacillus get the organism by the lungs, and it can pull it down with as much certainty as the staghound his prey when once he gets it by the throat.

Next upon the list comes the dread disease pneumonia, with nearly 20 per cent. of the entire lung mortality to its credit. A few years ago we should have found no support for, but in fact a contradiction of, our theory in the heavy death rate of this process, when it was regarded as an inflammatory and, in the old terminology, a typical "sthenic" disease. Now, however, we regard it as due to a lodgment and penetration into a vital organ of a germ which appears not infrequently present in the normal saliva; and its extraordinary preference for the lungs is probably again due to their character as a point of least resistance. Thus we have from 80 to 90 per cent. of the entire lung fatality due to two great diseases, whose chief determining factor is a lowered vital resistance.

Now let us look for a moment at the question of the favourite site or sites of disease in the lung. Is there any one part or region of the lung which clinical experience has shown to be more vulnerable or more frequently the starting-point of disease than any other? For the purposes of this inquiry I shall confine myself to the most frequent and important of the morbid processes—tuberculosis—partly because the changes in this have been more carefully and accurately studied, and largely also on account of the much more gradual and localised development of its symptoms. Pneumonia is as hard to localize as a prairie fire. In this case it is scarcely necessary to ask the question at the head of this paragraph. One of the commonest fundamental pathologic facts in our knowledge of tuberculosis is its extraordinary fondness for the apex of the lung. The proportions vary somewhat among different observers, but all declare that from 50 to 80 per cent. of all cases of pulmonary tuberculosis begin in the apex, and even the second-year student would instantly concentrate his attention chiefly upon this part of the lung in examining the case in which there was any suspicion of this disease. And the consensus of opinion also agrees that of the two apices the right is the more frequently affected in the proportion of about three to two. And the elaborate researches of Birch-Hirschfeld * have shown that the initial lesion of the disease is even more definitely localized, occurring in a majority of cases at the bifurcation of a particular bronchiole at the posterior part of the apical lobe.

From time immemorial most elaborate explanations have been advanced to account for this striking and, at first sight, singular preference. I say singular, because the apex is, in the first place, the smallest and most definitely limited region of the whole lung substance, and presents not a twentieth part of the area for infection which is offered by the base;

* Deutsche Archiv f. Klin. Med., Vol. 64.

and, secondly, because if the disease has any connection whatever with irritant or infectious materials, introduced in the inspired air, it is the last place in the world where we would expect, upon *a priori* grounds, that a lodgment or "settling" of these materials would be likely to take place. Even the bacilli and their spores are known to be ponderable and subject to the law of gravity, and would certainly tend to collect in greatest numbers and with greatest facility at the lowest instead of the highest part of the organ.

The same, of course, is true as regards the occurrence of congestion or stagnation of either the blood or lymph systems, although it has been gravely declared that certain peculiarities in the arrangement of the pulmonary veins are such as to prevent a proper drainage of this area of the lung, and cause it to be a point of deficient circulation, and consequently special pathologic liability. And this in the face of the fact that almost all hypostatic, congestive, or purely inflammatory processes begin at the posterior aspect of the lower third or base.

Another explanation which is offered is that in the apex we have a literal *cul-de-sac*, a point of "no way out here," for both blood and air. The statement must be admitted as perfectly correct. But is it any more true of this region than it would be of any part of the margin of the lung, whether anterior, posterior, or inferior? It is true it is a constricted and cone-shaped projection, but it is not one-half so compressed or "knife-edged" as any portion of the thin leaf-like inferior border, or the irregularly jagged anterior border, particularly on the left side. And it has the advantage of the whole influence of gravity in favour of the return of the blood, instead of against it, as in these other localities.

Last, and most weighty of all, we have the theory advanced that the apex is a point of least perfect expansion, and the air cells in consequence being less perfectly extended, are more liable to collapse or become filled with catarrhal or serous effusion. This purely mechanical version of the expansion theory is, I think, scarcely tenable. The cells of the lung are filled not by muscular force or circulatory energy, but simply by the pressure of the atmosphere; and while, if we were dealing with a fluid which had to be forced under pressure into every part, we might naturally expect that the highest portion of the cavity would be the one most likely to be imperfectly filled, yet when we remember that we are dealing with a gas, and a heated one at that, the probabilities are absolutely the reverse. Heated air tends, like any other gas, to seek and accumulate in, not the lowest but the highest point of its chamber, and, as far as the mechanical distention is concerned, the cells in the upper part of the lung in the neighbourhood of the apex would be more abundantly supplied with air than those in the middle or lower parts of the organ.

The other version, however, of this expansion theory is both rational and weighty, and it is, that owing to the constricted form of the chest at this point, the firmness and solidity of its bony walls, the absence of cartilage and limited movement of the first rib, and the pressure of the shoulder girdles and its great muscles, the normal respiratory rhythm is decidedly limited. Especially is this the case in sedentary occupations and in some forms of manual labour, such as digging, chopping, ploughing, &c., which tend to drag the shoulders forward. This view has been developed by Clough into the so-called "postural" theory of the disease. The normal expansive movements being imperfectly performed, there results a lowering of the general nutrition and the production of a sort of functional anæmia, which of course predisposes toward almost any kind of morbid process.

I would scarcely dispute that, in many cases at least, the stagnation in distention, which this theory supposes does actually exist, and is an important factor in the localization of the disease, and yet I am inclined to doubt whether the actual state of activity of the apex has not been very much underestimated. It is perfectly true, of course, that the bony framework of this part of the chest is both limited and rigid, as compared with the lower regions. But when we remember that we are dealing, as we have already seen, with a heated gas and not with a fluid, and that the whole elastic resiliency and weight of the entire chest wall will, at each expiration, expend itself not only upon driving the air out of the trachea, but also to some degree up into the apices; and, further, that while this portion of the chest has firm lateral boundaries, it has no definite roof, and that the pleural cavity actually extends from three-fourths of an inch to one and one-half inches above the border of the first rib, we shall, I think, be justified in questioning whether the immobility of this part of the lung has not been unduly insisted upon.

It is of course difficult to get actual observations upon this point, for the reason that after post-mortem rigidity has set in, the elastic and continually changing roof of the pleural dome becomes as rigid and unyielding as its bony walls, and even artificial respiration is but a poor substitute in such instances as this for the natural process. I happen, however, to have seen personally two operations in the surgical clinic for the removal of huge masses of (tuberculous) cervical glands, in the process of which the upper aspect of the pleural sac was freely exposed, and the way in which it plunged up and down with the respiratory rhythm was little short of appalling, and seriously added to the risks of the operation and the possibility of an accidental puncture by the surgeon's knife. In one case, in a child of about seven, the membrane appeared to have a range in the vertical direction of at least an inch, if not an inch and a half, although, seen at the bottom of a gaping wound in the neck, half filled with blood, its real range would appear distinctly exaggerated. Be this as it may, I think I am justified in declaring that neither this theory nor any other which has heretofore been proposed is really adequate to satisfactorily account for the extraordinarily high morbid liability of this region of the lung.

When, however, we turn to morphology, we are instantly confronted with the striking and suggestive fact that the apex is precisely the point at which the most active change in the area of the lung is taking place, and hence is again the point of greatest instability and lowered vital resistance. It is, I think, generally admitted that while the respiratory cavity in mammals is undergoing progressive limitation at both its cephalic and caudal extremities, in man at least, these changes are most active at the cephalic end. This is shown, first, in the not infrequent persistence in adult life, and constant appearance in the embryo, of cervical ribs upon one or both sides; second, in the not infrequent atrophy of the first rib, and, in the internal structure of the lung, in the disappearance of the eparterial system of bronchi. Upon the left side this disappearance is complete, but upon the right side atrophic traces of the system still linger, in the shape of the upper or so-called first lobe, and it is, as we have seen, precisely in this lobe that 60 or 70 per cent. of cases of apical tubercle have their origin. In other words, we have the disease most frequently beginning in that part of the lung which is undergoing the greatest amount of ancestral retrogression, and especially frequent upon that side in which there is still an atrophied remnant of the former development. In fact, I regard tuberculosis as a disease preferring not only the most unstable organ in the body, but the most unstable regions of that organ, and of those regions that side of the median line in which retrogression is still going on. It attacks the weakest side of the weakest part of the weakest organ in the body.

Of course I am aware that the objection will at once be raised that the vestigeal or degenerate nature of this lobe is by no means satisfactorily proved, although the preponderance of investigations and authority appears to point decidedly in that direction. Abey, for instance, from his most careful and elaborate studies of the question, has come most decidedly to the conclusion that the right upper lobe has no remaining counterpart upon the left side, and although Hasse's further investigations have rather supported the view that a process of onward growth headward has been taking place in the human lung, of which the right upper lobe is the first result, yet Weber, LeBouck, and Howes have brought forward considerations which decidedly support the original view of Abey.

Unfortunately the ontogeny of man throws but little light upon the question as to whether a symmetrically trilobed lung, with paired eparterial lobes, was the ancestral condition or not, although three cases of a pair of eparterial lobes in man have been reported by Dalla Rosa. Indeed, the arrangement of the lungs, as to symmetry, throughout the mammalian kingdom is, apparently, of the most arbitrary and uncertain character. In a few species, for instance, Bradypus, Equus, Elephas, and Phoca, there is a paired eparterial lobe. But these can hardly be regarded as ancestral or specially primitive forms; nor does there seem to be any possible relation between the phylogeny or the environment of the various forms which will account for either their symmetry or lack of it. In Hystrix, for instance, both the eparterial lobes and their bronchi disappear completely.

Nor does our pre-mammalian ancestry throw any further light upon the problem, except that in their very earliest appearance, in Dipnoi (Lung-fishes), the dividing of the lungs begins at the posterior extremity, the anterior extremities remaining united, and hence the anterior lobes might be regarded as the newest part of the lung. Almost the moment we land among the amphibia, and still more frequently in reptiles, the symmetry which is originally present begins to disappear, sometimes in favour of the one lung and sometimes of the other, though in the great majority of cases we find the interesting and possibly suggestive condition that the left lung is the one which begins to atrophy, and in some snakes almost totally disappears. It would, of course, be a very far cry to say that this ancestral preponderance of the right lung had any bearing upon the marked mammalian tendency for the supernumerary lobe to be retained upon the right side, which we know to be the condition in the vast majority of cases.

The great name of Wiedersheim must also be added to the support of the "vestigeal" theory of the right cephalic lobe, and the impression is strong from a general view of the entire field that a bilateral symmetry was the original condition of affairs, and that where that symmetry was disturbed the great tendency was for this to occur at the expense of the left lung. As I have said, this is still a disputed question, and Hasse and one or two other investigators of highest standing in Germany are decidedly of the opinion that it represents a new growth, and Huntington's studies in this direction have led him to the same conclusion. However, for the purposes of this discussion, it makes but little difference which view is accepted, all that my postulate requires being that the region should be in a condition of marked instability, which of course would be true in either case.

I stated just a moment ago that there appeared to be no connection whatever between the life and habits of any of the mammals and the development of this part of the lung, and so far as balance between the two apices is concerned this is true, but not as to the proportion between this part of the lung and the base in some of the species. Although there are many exceptions, it may, I think, be laid down as a general rule, and indeed I have the high authority of Dr. Huntington for the statement, that the proportional development of the cephalic end of the lung is, if we might use the expression, in excess of the normal in the ungulates, and particularly in the Bovidæ and the Cervidæ, while, generally speaking, it is below the average in the carnivora. The suggestion has occurred to my mind that probably this condition may be due in the graminivora to the constant pressure exerted upon the base of the lung by the enormously distended paunch, which pressure is so great that, as we have seen, in certain forms of gastritis (rumenitis), and also of colitis in cattle and horses, respiration will be sc seriously interfered with as to produce fatal asphyxia, and rupture of the diaphragm may even result. Be this as it may, we are justified, I think, in stating that the posterior or caudal extremity of the lung in ungulates is to be regarded as the point of the greatest tendency to recession.

And here we have what is to my mind an interesting and suggestive coincidence that in domestic cattle one of the points of most frequent attack and initial pulmonary lesion of tuberculosis is in the dorso-caudal lobe, though not in the same preponderance as in the apex of the human lung. It would be interesting to compare the morbidity of the different extremities of the lung in the carnivora or in the horse with his double eparterial lobe, but unfortunately for our purposes both of these are largely immune to tuberculosis. But it certainly seems a singular coincidence, if nothing more, that this typical disease of lowered resistance should attack in its two principal victims, the human and bovine families, just that part of the lung which lies at a disadvantage either ancestrally or mechanically.

There is one other disease of the lung which we might almost be justified in regarding as ancestral, and that is emphysema. It has always been something of a puzzle to pathologists why, when almost every other organ in the body, if inflamed, undergoes either actual solidification or atrophic or sclerotic changes, due to fibroid degeneration with shrinking in bulk, the lung, on the other hand, displays a tendency, under almost any form of chronic irritation, to pursue exactly the opposite course and to become lighter and more expanded. Fully to explain this rarefaction, neither the usually assigned "back pressure" of cough, nor the gasping respiration of asthma, is of itself quite adequate. When, however, we remember that one or more of these causes, are acting upon a web of delicate and complex tissue,—when we recall the method in which that tissue has very gradually grown, by folding, refolding, and meshing, from a simple smooth-walled, distended, epithelial sac, such as is still found in the frog and mud-fish,—then we can, I think, hardly avoid the impression that the rarefaction and expansion of the lung in emphysema, is a reversion to a remote ancestral stage. Thus this apparently exceptional phenomenon, ceasing to be unique, would fall naturally in line with so many other morbid processes.

No other hollow organ in the body tends to become lighter and more expanded under the influence of chronic inflammation, and no other organ has a similar pedigree. Fothergill has advanced an almost similar suggestion, stating that the "barrel-chest" of chronic bronchitis or asthma was a reproduction of the turtle lung with its expanded air-cells and rigid chest wall; and while the suggestion of the last clause appears at first sight an almost whimsical one, yet we have grounds for believing, as I hope to show in the next chapter, that even the fixed and rigid chest-wall, not merely of the asthmatic, but also of the consumptive, has an ancestral basis.

CHAPTER V.

THE DEFORMITIES OF THE CHEST IN THE LIGHT OF ITS ANCESTRY AND GROWTH.

THE chief deformities of the chest may apparently be divided into two distinct classes, those in which the transverse diameter is increased at the expense of the antero-posterior, which for the sake of brevity in discussion we will call the transverse or "bellows" form of chest, and those in which the increase appears to be in the antero-posterior diameter and the contraction in the transverse, which again, for the sake of brevity, we will call the antero-posterior or quadrupedal type of chest. It is obvious that these increases and diminutions of the diameters are relative rather than absolute, and that when we say that a chest is flattened, what we mean is not so much that its antero-posterior diameter is absolutely diminished, as that this is short in comparison with or relative to the transverse diameter, and *vice versa* in regard to the antero-posterior chest. In fact, the deformities of the chest would appear to depend upon a flattening or compression in the antero-posterior diameter and bulging in the transverse, or *vice versa*.

In the transverse or "bellows" class of chests, we would place the innumerable varieties of flat chest, "hollow chest" as it is often termed, and the singular "Funnel chest"; while under the antero-posterior type would be placed the pigeon breast and guttered, or grooved, sternum. It would also appear that these two divisions corresponded fairly accurately to the two great types of chest among the mammalia. The one, the typical quadrupedal chest—as found in the carnivora, the ungulates, and the great majority of mammals—has an antero-posterior diameter which is distinctly in excess of the transverse, so that a transverse section of the chest cavity would form an oval or heart-shaped figure with its long diameter perpendicular to the anterior wall (sagittal).

This form of chest is obviously necessitated by and correlated with the backward and forward swing of the anterior limbs, in the movements of locomotion. Maximum capacity with minimum width, so far as this may be consistent with abundance of room for the heart and great vessels, is the desideratum. This is attained by narrowing, deepening, and almost immobilizing the anterior third of the chest, leaving most of the costal respiration to be carried only by the "heaving" lateral expansion of the sides of the chest behind the shoulder girdle. In the quadruped the chest-bellows is turned upon its edge, if we may use the expression, and the flaps play laterally. In the erect chest the bellows have been rotated at right angles to their original position, and the flaps play antero-posteriorly. This quadrupedal type of chest has passed into popular literature as the well-known "deep" chest of the hound or the race-horse; and it is very curious to note to what an extent, by a process of transference, terms which are descriptive of this form of chest have been applied to the human torso, where, as we shall see, they are anything but appropriate.

The other type of chest is that in which the transverse diameter equals or exceeds the antero-posterior. It is found only in certain members of three widely separate families, but aberrant order of bats, the whales, and the higher primates, the anthropoid apes and man. So striking was this departure from the common type that the bats were actually placed in close relation to man, in the old Linnean system. Here again, however, a mechanical explanation would appear to be adequate to account for the form. The three families have absolutely nothing in common, save the fact that the anterior limbs are no longer used for supporting the body during ground locomotion, in the bats being used for flight, in the whale as "fins," and in the anthropoids and earliest man for swinging through the branches. Thus there is no longer a limited backward and forward movement of the limbs in parallel lines, so that the "keel" or boat-shaped form of chest is no longer a necessity, and the great sheet of the pectoral muscles, using the wing in the one case and the hand with the branch it has seized, in the other, as its fixed point, is continually pulling the prominent sternum back toward the vertebral column. The ribs yield at their angle and we have the anteroposterior chest gradually transforming itself into the transverse form.

The bird, it may be said in passing, solves the problem in a somewhat different way by the development of an enormous keel or crest on the sternum, the actual chest wall itself remaining, however, in very much the primitive shape, with only a slight preponderance of the anteroposterior over the transverse diameter. After the upright position has been attained this modification goes still further. The arms hang by the sides instead of being permanently extended in a forward or dorsi-ventral direction. The shoulder-girdle, with its great mass of muscles and attached limbs, sinks downward from its former position and begins to press more or less firmly upon the lateral aspects of the lower part of the chest wall, the first joint of the limb lies parallel and in contact with almost the entire lateral border of the chest. As a result, the lateral expansion of the wings of the chest is interfered with by the pressure and the presence of a joint of the limb in this situation. But the lateral expansion is the chief factor in quadrupedal costal respiration, as can be shown in the heaving flanks of the race-horse or of the hound after the chase. The anterior aspect of the chest, having been completely freed from the former splint-like action of the limbs, begins to become the most freely movable part of the wall, and we have the rising and falling or antero-posterior type of respiration to a large extent substituted for the lateral or wing-like type.

To afford still greater freedom for this, the girdle and its scapulæ recede toward the vertebral column until they come, ultimately, to lie almost directly on the flattened posterior wall of the chest. In fact, the chest comes to act like a pair of bellows, of which the vertebral wall is the fixed and the sternal wall the movable flap. I am convinced that one of the most important factors in the proper respiratory development and capacity of the human chest is the extent to which the scapulæ come to lie upon the posterior wall or fixed flap of the bellows.

The type of vigour in the human chest is a broad, flat thorax, instead of a "deep" one. "Depth" is a sign of arrested development.

To adopt a rough mechanical simile, the flaps of the human chest-bellows have been "turned round" so as to move at right angles to their former play. Instead of the chest expanding chiefly by "wing" movement *behind* the shoulder girdle, and by the descent of the diaphragm, the whole anterior wall sways up and down *between* the scapulæ, and costal respiration almost equals diaphragmatic. Quadrupedal respiration is chiefly diaphragmatic and lower costal.

And both infantile and late consumptive respiration are of a curiously similar type.

But, what has all this purely morphologic process to do with us as physicians? Even if it be granted that the human chest, in the course of its development from an earlier quadrupedal form, has passed through these various stages from the keeled to the bellows type, how does this bear upon our study of the human chest in the nineteenth century? Much in every way, for the reason that not merely do the probabilities point strongly to our human chest having passed through such stages ancestrally, but every individual chest passes through a number of these stages under our very eyes. In the embryo at the fourth month we have a chest which is almost identical in type with that of the quadruped—the dog, for instance, in which the antero-posterior diameter is as three to two, although it seldom reaches this figure in the embryo. Morris simply gives it as "greater." Macalister says, "the chest is deeper sagitally than transversely." At birth the diameters have come up to the proportion of the lower apes, in which they are almost equal, while from this period up to the twelfth or thirteenth year and to the twenty-fifth even, there is a gradual, steady modification of the chest shape until the full adult "bellows" form is reached, in which the diameters are exactly reversed, viz., as two to three in favour of the transverse. Although, according to Rotch, the proportion is as high as 1 to 2.5 or 3 (D. Powell). Though these changes in proportions are matters of common knowledge and are given in most of our anatomic works, I have been unable to find the exact records upon which the statements are based, and hence have been obliged to depend upon my own few measurements of embryonic chests, in six of which, between the fourth and ninth months, the average proportion between the antero-posterior and transverse diameters was as 101 to 100. (*See* Tables.) In an embryo at the fourth month it was as 110 to 100.

I was also greatly surprised to find, on first taking up the question two years ago, that no recognized normal or standard relation between these two diameters in the human species had yet been established. As it seemed to me that the determination of such a relation, or *Chest Index*, would be of both scientific and practical value, and a careful search through the literature, with the courteous assistance of Professors Macalister, Wilder, Huntington and other leading anatomists, proving fruitless, I proceeded to collect data, and make measurements with this end in view.

A few statements of proportion are given, but nearly all of them are *internal*, like that of D. Powell quoted above, and, of course, impossible of ascertainment upon the living subject.

My measurements were all taken with calipers, at the level of the nipples; one point resting upon the sternum, the other upon the dorsal spinous process horizontally opposite. In my earlier measurements, I took the diameters at three levels, the sternal notch, the nipple, and the tip of the ensiform cartilage, but soon abandoned the first, because it was practically impossible to get a transverse measurement at that level, and the last because the antero-posterior diameter varied so widely, according to the slope of the ensiform and lower third of the sternum, as to furnish no true index of chest form. My first short series was made upon internes and students in the Buffalo General Hospital, my second upon the internes in the military hospital at Fort Porter, and my third, and most valuable, through the kindness and valuable assistance of Surgeon-Major Appel, upon fifty United States regulars in garrison at Fort Porter.

Table 1.

NORMAL CHEST MEASUREMENT—INCHES.

ENLISTED MEN. FORT PORTER.

Number.	Age.	Weight.	Inches Height.	Extramammillary Length.	Suprasternal Depth.	Nipples.		Ensiform.		Index.	
						Ant.	Trans.	Ant.	Trans.	Length.	Breadth
1	31	146	68·5	11	6	8·2	10·8	7·1	10·5	98	76
2	42	165	68·5	11·2	7	9·2	11·3	9·5	11·2	101	81
3	40	155	64	10·5	6·5	8·6	11·5	8·5	11·3	109	74
4	24	158	69 5	14	6·2	8·3	10·5	8·5	11	75	79
5	37	174	70	14	6·2	8	12	8·3	11·5	86	67
6	23	163	71	12·6	6	8·2	11·4	7·5	12	90	72
7	28	164	71	13·2	5·6	7·2	11·5	7	11·5	87	63
8	43	160	66	12·5	7·2	9·5	12·5	9·2	11·5	100	76
9	26	162	68	12	6	8·2	10·5	8·2	11	87	78
10	29	135	65	11·8	5·6	8	10·5	8	10·5	89	76
11	36	130	64	11·6	6	8·2	9·5	8	10	82	86
12	38	218	73	12·6	7	9·8	12·6	9·5	12	100	77
13	25	138	68·5	13	6·2	8·5	10·5	8·6	10·5	81	81
14	21	137	67	12	5·5	8	11	8·6	10·8	92	73
15	27	178	72	13·8	6·5	9	12·3	8·2	12·2	93	73
16	38	140	67	13	6	8	10·6	8	11	82	75
17	34	142	70·5	13·5	6·3	8·5	10·5	8·8	10·2	78	81
18	28	158	68·5	13·6	6	8·2	12	8·5	11·6	88	68
19	29	130	66·5	12 2	6	8 5	10·5	8·2	10·5	85	81
20	29	154	66·25	12·5	6	7·5	10·6	7·5	11·2	85	70
21	31	128	68·75	12·2	5·5	7·5	11·5	7·5	11·5	94	65
22	22	132	67·5	12 5	6	8	10·6	7·5	10·8	85	75
23	24	134	65·25	12	6	8	11	8	11	92	73
24	46	150	65·5	13	6	8	11·5	8	11·2	85	69
25	27	152	68·25	12·5	6	8	10·8	7 5	11·2	86	74
26	24	130	66·25	12	5·5	8·8	10·2	9	10·5	84	86
27	28	141	68·5	13 5	5·5	8·2	9·6	8·5	9·5	71	85
28	44	138	65·5	11	6	8·5	11·5	9	11·5	104	73
29	26	149	66·5	12	6	8	12	8	11·5	100	69
30	25	147	66·5	12	6	8	11	8	11·4	92	73
31	32	142	65·5	13	6	8	11	8	11·2	83	73
32	26	140	67	11·5	6	7	11·3	7	11	98	62
33	26	128	68	13	5·6	7·5	10·2	7	10·5	78	73
34	44	174	65·75	11·5	6·5	9·6	11·7	9·5	11·5	102	82
35	38	152	71	13	6	8	11·3	7·5	11·2	81	71
36	28	175	68	12	6·5	9·2	12	9	11·6	100	76
37	30	136	68·5	13·5	5·6	8·2	11·2	8·2	11	83	73
38	36	139	69·5	12·6	6	7·5	10	7·5	10	78	75
39	27	140	66·5	12	6	8	10	8	11	83	80
40	31	144	68	13	6	7 5	11·2	7·6	11·6	80	61
41	33	130	68·25	13·6	5·5	7·5	10·6	7·6	11	78	71
42	29	160	66·75	11·6	5·7	8·2	11·1	8·2	11·2	86	74
43	26	140	66·5	12·5	5·6	7·3	10·6	7	11	85	69
44	22	134	67·25	14·2	5·5	7·1	11	7·5	11	77	65
45	26	154	67·25	13·5	6·3	8·2	10·7	8·2	11	78	77
46	26	130	65·75	13	6·6	8·5	10·5	8·2	10·5	81	81
47	27	140	66·5	13	6·2	8	11·3	7·6	11·2	81	71
48	31	136	67	12·2	6	8	11·2	8	11	92	72
49	26	130	65·75	13	5·6	7·6	10·5	8	11	81	72
50	28	140	67	13·2	5·8	7·8	11	7·5	11·2	83	71
						Average Indices...............				87·3	73·6

A few months later, I was fortunate enough to secure measurements in these diameters, at the nipple level, of 2,300 Yale College students, taken by Dr. Seager, in connection with their gymnasium examination.

These two independent series, as seen by the table appended, harmonize remarkably closely; and, I think, we may feel justified in fixing 71 as a fairly accurate approach to the normal, or standard, adult human *Chest Index*.

TABLE II.

Normal Adults.	Breadth Index
Internes Buffalo General Hospital	71·5
" " Garrison "	72·6
Enlisted Men (50)	73·6
2300 Yale Students	70·0
General Average—Normal Chests	71·0
" " 82 Tuberculous "	79·5

Average Diameters.	At Nipple. Ant. post.	Trans.
Enlisted Men	8·0 in.	11·0 in.
Yale Students	7·5 "	10·7 "
	7·6 in.	10·8 in.
40 Tuberculous Patients (Buffalo)..	8·4 in.	10·5 in.
42 " " (Brompton)	8·0 "	10·1 "
Tubercular Average ..	8·2 in.	10·3 in.

This adult *Index* of 71 is a decided change from the fœtal Index of 101, and the next thing to be determined is the rate at which the transition takes place, and I have accordingly taken measurements of some fifty infants and children with the results shown in the table.

TABLE III.

Series of Breadth-Indices.

Fœtal Chests (6)	Average	101
Infants under 2 yrs. (18)	„	94
Children 2 yrs. to 9 yrs. (20)	„	86
Boys 14 yrs. to 19 yrs. (12)	„	81
Adults 17 yrs. to 44 yrs. (2370) ..	„	71
82 Tuberculous Cases	79·5	
30 "Flat" Chests	80·0	

As will be seen, there is a steady progress from the nearly circular chest at birth to the flat chest of the adult; and as in the ancestral series, the rounder the chest the more important the part played by the diaphragm in respiration. The "prize-fighter" chest of the new-born infant, which proud mothers are so sure is an indication of "a strong constitution," is quite limited in its costal movements, and infantile respiration is chiefly abdominal.

Now, as to the shape of the tubercular chest, and its position in this series. There is a surprising unanimity of statement among authorities, both anatomical and pathological, that it is flat, or has its antero-posterior diameter diminished. Usually, however, no measurements are given, except circumferences. And, I may frankly confess that when I began these measurements I was fully under the impression that I should find the tubercular chest an exaggeration of the normal adult form, with a diminished antero-posterior diameter, and a low index.

To my surprise, however, my first measurements showed exactly the reverse condition. Every additional measurement confirmed the first, and although I have only succeeded, so far, in collecting, by slow degrees, the dimensions of eighty-two tuberculous chests, yet they are a singularly uniform series. Forty of these were taken in Buffalo Hospitals, through the courtesy of my colleagues, and forty-two were

Table IV.

CHEST DIMENSIONS.

Number.	Brompton, July, 1899.	Stage.	Ant.-p.	Trans.	Length.	Br. Index.
	Men—					
1	H. H. ... æt. 14 yrs.	2	6·7	8·3	9·7	81
2	T. N....... „ 38 „	1	7·8	9·5	11·2	82
3	J. J. .... „ 43 „	2	7·9	10·6	11·2	75
4	T. P....... „ 37 „	3	7·9	10·4	12·3	76
5	A. C ...... „ 19 „	3	7·9	9·7	12	81
6	G. M. ... „ 22 „	2	6·9	9·9	13·2	70
7	H. M. ... „ 26 „	3	8·3	9·6	11·9	86
8	A. A....... „ 31 „	1	7·9	10·3	13·8	77
9	A. H....... „ 20 „	2	7·6	10	12·6	76
10	W. S. ... „ 34 „	3	7·8	9·3	12·7	84
11	E. W. ... „ 41 „	4	8·8	9·6	12·3	91
12	W. E. ... „ 23 „	1	7·5	9·6	12·8	80
13	C. B....... „ 42 „	2	8·6	10·4	13·1	83
14	J. H....... „ 36 „	3	8·3	9·7	12·4	86
15	C. S. .... „ 42 „	2	9·4	10·4	11·7	90
16	I. C. ...... „ 40 „	2	8	10·2	13	80
17	C. C. ...... „ 46 „ ?	1	8·8	11·3	11	80
18	E. E....... „ 42 „	2	8·2	10·3	12·3	80
19	T. C. ...... „ 43 „	3	7·7	11·6	13·6	70
20	T. P....... „ 25 „	3	7	9·5	12·1	74
21	G. C....... „ 38 „	1	7·8	9·7	11·3	80
22	H. C....... „ 26 „	2	7·8	10·3	12·7	76
23	W. H. ... „ 31 „	3	8·3	10·6	12·6	80
24	W. S. ... „ 26 „	3	8·5	11	10·6	77
25	T. W. ... „ 40 „	2	8·5	10·3	11·7	83
26	S. H....... „ 19 „	1	8·1	10·5	13·1	80
27	F. F....... „ 40 „	1	8·7	11·2	13·1	80
28	J. P. ...... „ 37 „	3	8·6	10·7	12·7	80
29	C. W. ... „ 21 „	2	8·3	9·7	10·8	86
30	W. M. ... „ 35 „	1	8·6	10·7	13	80
31	T. O....... „ 30 „	1	7·9	10·5	12·1	75
32	P. P....... „ 21 „	1	7·7	9·7	12·7	80
33	S. G ...... „ 36 „	3	7·7	10·3	12·7	75
34	A. F....... „ 38 „	2	7·1	10·2	11	70
35	G. Mc. ... „ 32 „	1	9·3	10·8	13	90
36	J. S. ...... „ 25 „	2	7·3	10·5	13·7	70
37	W. L. ... „ 31 „	2	9	9·6	12·1	94
38	H. B....... „ 21 „	3	8·2	9·5	12	86
39	O. B....... „ 23 „	3	7·1	9·6	13·8	74
40	J. M....... „ 19 „	1	7·2	10·7	13·5	67
	Total	......	1040	......	......	3185
	Average (40)	......	8·0	10·1	12·4	
	Breadth Index ...	......	......	......	......	79·6
	Length „ ...	......	......	......	......	81·4
	Women—					
1	E. J. ..... æt. 22 yrs.	3	7·6	8·3	10·3	92
2	A. R....... „ 30 „	3	7·1	10·1	11·8	70

taken at the Brompton Hospital for Diseases of the Chest by the courteous permission of Drs. Green, Acland, Fowler and Kidd, and with the kind co-operation of the Resident Medical Officer, Dr. Felkin, and my friend, Dr. Conner.

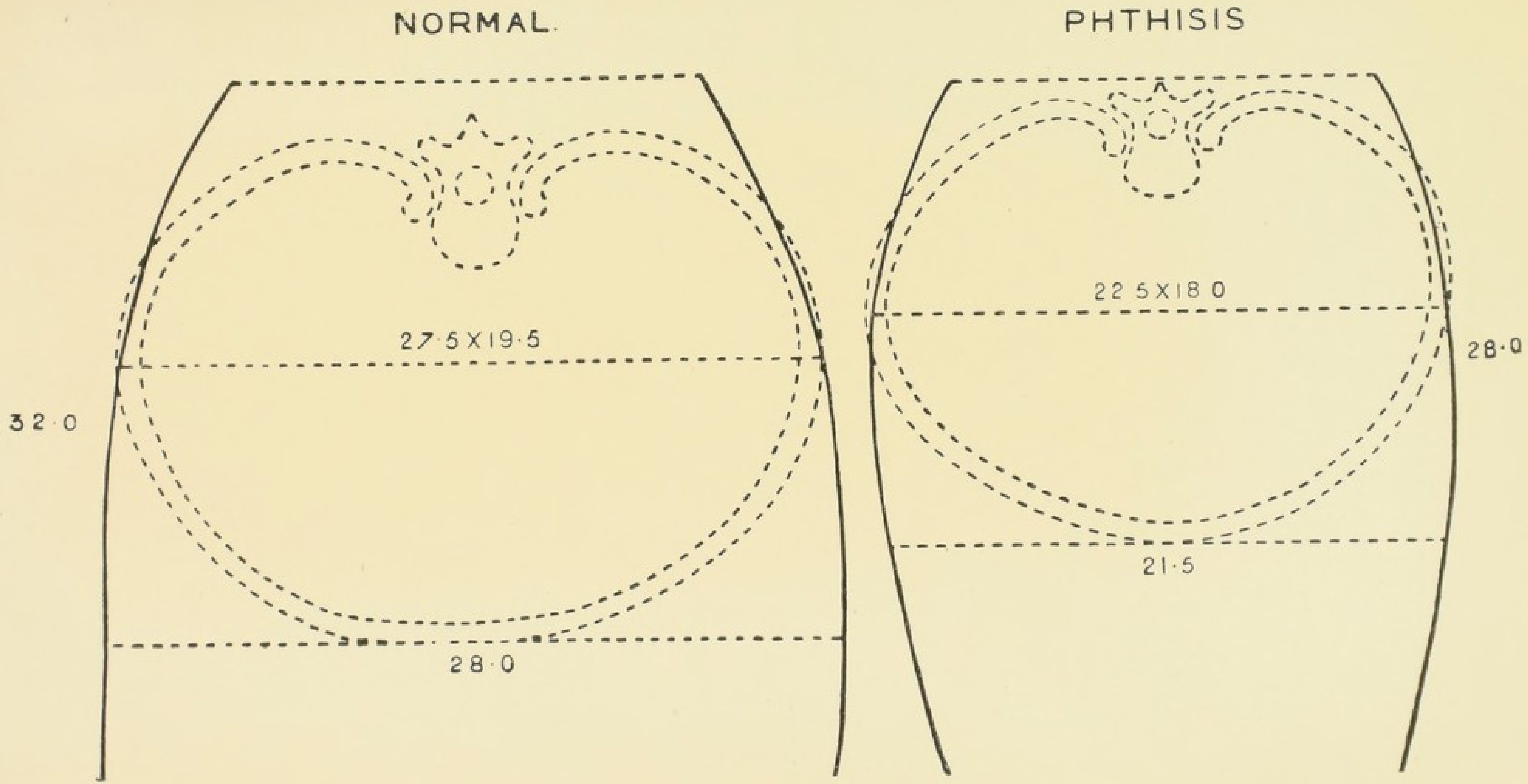
The results of the two series agree so closely that their average *Index* of practically 80 (79·5) may, I think, be regarded as indicating fairly correctly that of the tubercular type of chest. The average *Index* of the American cases was 79·4, and that of the English 79·6.

As shown in the tables, the antero-posterior diameter in the Buffalo series instead of being diminished was 0·8 in. *above* the normal average of 7·6 in., while that in the Brompton series was 0·4 in. above the average. The transverse diameter in both is found to be *below* the average 0·3 in. in the American cases, and 0·7 in. in the English series. Thus making the average "depth" of all these chests 0·6 in. above the average, and their average breadth 0·5 in. below it. So that the typical tubercular chest would appear to be *round* instead of flat.

The uniformity of the individual measurements in both series strengthens their claim to be regarded as typical. Out of the Buffalo series only five chests reached or fell below the normal index, and in Brompton series only six, or eleven out of eighty-two. Of the forty Brompton male cases, twenty-five lie between 75 and 85, or 62 per cent. There would certainly seem to be some sort of connection between this type, or form, of chest and pulmonary tuberculosis.

But if the tubercular chest is really round, how has it come to be universally described as flat? Simply, I think, from the position taken by the shoulders in this type of chest. The more carefully one inspects chests of this class, the more one is struck with the extent to which this flatten-

Indexes of Thoracic Breadth in Health and in Tuberculosis.



ing is apparent and not real. In the first place, even in popular terminology, the "flat" chest is almost invariably associated with "round" shoulders. In other words, the flattening of the anterior aspect of the chest is in very large measure due to the forward movement and carrying of the great muscular masses of the shoulder girdles. Our standard of flatness or fulness of chest is simply a line drawn across it from one acromion process to the other, and it is obvious that we may have a distinct flattening of this line, with a decidedly round chest, provided that the shoulders have rolled forward far enough. As is already suggested in the term round-shouldered, a mere glance at the hollow chest will show us that a very large proportion of this anterior flattening is due to the gliding forward of the scapulæ and their appendages, so that the posterior outline of the upper part of the chest wall, instead of being almost a straight line as it should in the ideal position, is a very decided curve. And, upon taking actual measurements, we find ourselves confronted by the surprising situation that our so-called flat chest is really, if anything, slightly above the normal in its antero-posterior diameter, as is shown by the above figures.

How is this extraordinary optical illusion brought about? Not only is there no inconsistency between the facts, but one is necessarily a consequence of the other. My attention was first called to this relation in examining the chests of some school children who were undergoing special gymnastic exercise for the purpose of overcoming round-shoulderedness. The appearance of the youngsters was characteristic; the chest was flat, the back and shoulders bowed or rounded, the arms swinging slightly in front of the median line in a characteristically anthropoid position. Upon taking hold of the children by the shoulders, from behind, and gently but firmly pulling the shoulders backward, while the spine was supported by the knee, it was found that an apparently normal shape of chest could be produced; but the difficulty was that the shoulders would not stay in this position, and a little further experimentation and some measurements revealed that the chest was so nearly round, that the scapulæ had no flat posterior surface to rest upon, but were continually sliding forward upon the barrel-like outline of the outer surface of the ribs. This tendency was assisted by the somewhat slouching or anthropoid attitude, which boys are apt to assume, and by the contraction of the great pectoral muscles. So marked was this latter fact that, in the language of their gymnasium teacher, they were said to be "muscle-bound," and I found upon inquiry that the trainer was quite familiar with this condition of affairs, and recognized it as a frequent factor in the production of this type of chest and shoulder. In short, the round chest, from the very insecurity of the position which it affords to the inner aspect of the scapulæ, tends to become, under the influence of gravitation and dominant muscle action, the apparently flat chest. In the case of children it is an amusing coincidence that when I asked the trainer what forms of exercise were found to be most useful in correcting this defect, I was immediately told that all sorts of climbing exercises, especially those which were done with the back toward the ladder, rope or framework which was being climbed, were most useful. In other words, by a reversion to the arboreal habits of our ancestors, who possessed this form of chest, its progress into the higher form can be expedited.

In most consumptive chests the "flatness" can be made to disappear completely by the same simple manipulation of pulling the shoulders backwards. And the projection of the lower angles of the scapulæ, giving rise to the so-called "winged chest" of the consumptive, is largely due to the rounding of the posterior wall of the chest and consequent absence of any flat surface upon which they may rest securely and easily.

An amusing instance of this optical illusion is to be seen in a well-known work on physical diagnosis. The usual statement as to the flatness of the tubercular chest is given, and photographs of a strikingly typical case are appended.

Fortunately, both a front and side view of the patient are given, and, as these are of uniform size and focus, the actual proportion can be determined by careful measurement with a finely graduated rule. And the *Index* is seventy-eight, or *seven degrees above the normal*, and only one and a half degree below the consumptive average!

And now comes the most important question of the problem. Is this form of chest the result of the disease, or does it precede it? Graphically speaking, does the chest cause the disease, or the disease the chest? To this no positive answer can be given in the present state of our knowledge, as it would require a large number of measurements taken in the earliest appreciable stage of the disease, or really, to be perfectly conclusive, measurements of a large number of boys or girls between twelve years and twenty-one years of age, and then keeping them under observation for ten years to see how many of the round-chested ones became tuberculous, as compared with the normal.

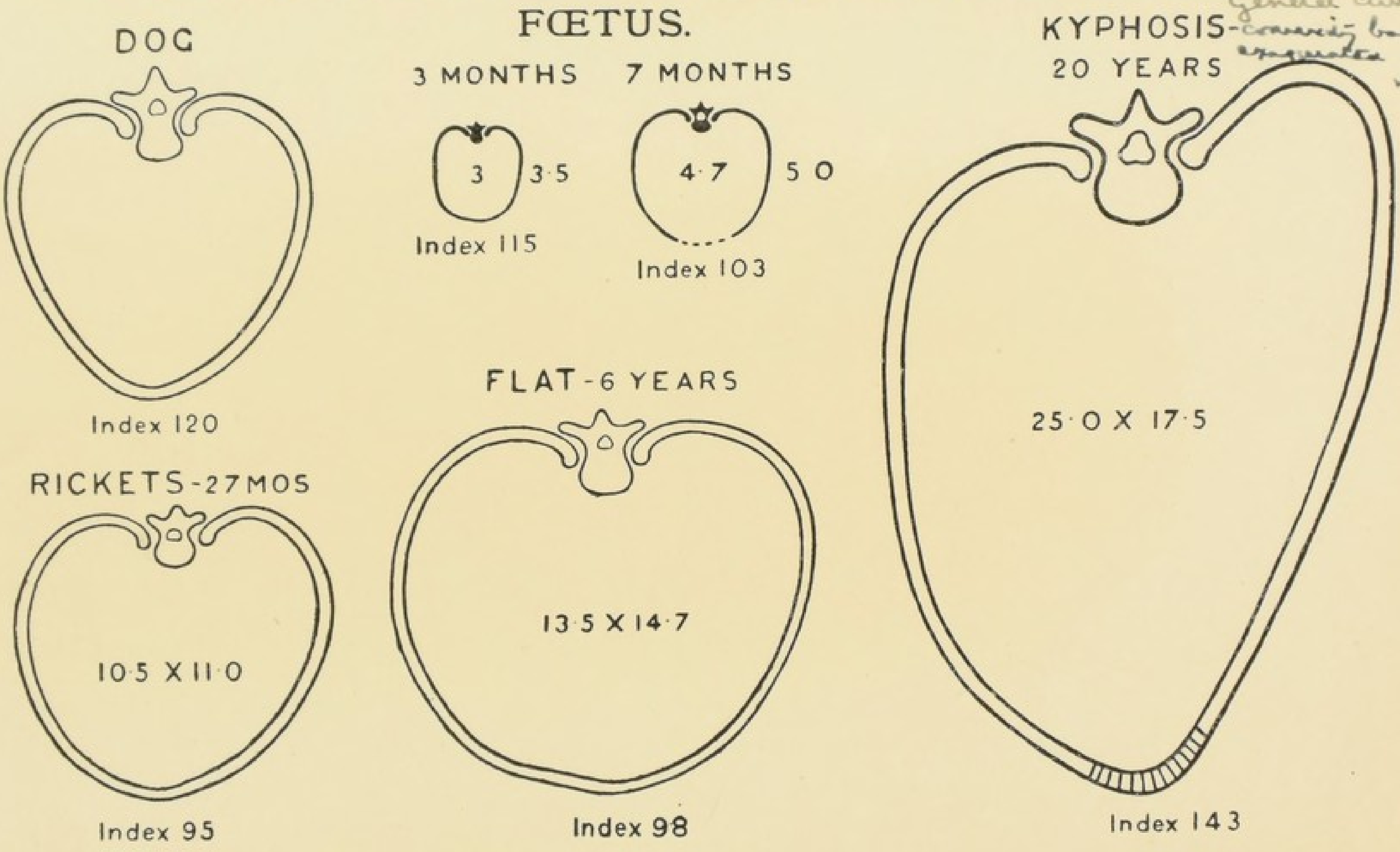
There are, however, several considerations which render it strongly probable to my mind, that the shape of the chest precedes the disease, and is a predisposing factor. First of all, such measurements as I have been able to take in the early stage of the disease show an already high Index. Four of the Buffalo cases were in the first stage of the disease, and of the Brompton series twelve, and the average Index of these was 79·2, only ·4 of a degree below the general average. I think there is little question that the deformity tends to increase slightly during the disease, as the chest gets pulled up into a permanent position of extreme inspiration.

In the second place, all that is required to produce this type of chest is that its form-development should be arrested at about the fifteenth year, when, as we have seen, the chest has normally an index of about 80. And as this form is present in all non-tubercular cases of "flat" chest which I have been able to measure, some thirty in all, and nearly all backward or defective children measured have an Index higher than that normal at their age, I believe that such an arrest has occurred in most tubercular cases.

Finally, such an arrest of development, by keeping the free anterior flap of the chest-bellows encumbered at its sides, and even in front, by the shoulder masses and arms, would seriously hamper the proper expansion of the lung, and render it much more liable to the attacks of the disease. While it is difficult to conceive how pulmonary tuberculosis could within a few months change a chest of normal form to one of 10 degrees out of the normal.

The shape of the tubercular chest also departs from the normal in another dimension, and that is, its length. This is slightly but distinctly in excess of the normal, both absolutely and relatively, averaging in my eighty-two cases 12·8 in., and in the soldiers and students 12·3 in. In all these, the measurements were taken from the centre of the clavicle to the lowest point of the costal cartilages, intersected by a line drawn just outside of the nipple. I found that the slope of the lower ribs varied so much that measurements to a certain rib, or cartilage, bore no constant relation to the actual length of the chest. While the absolute increase was slight,

Thoracic Indexes in Dog and Man; Compared Effects of Development and Disease.



the relative or Index excess over the normal was well marked. In the normal chests this index averaged 87·5, in the tubercular 80·5, the length of the chest being taken as 100.

TABLE V.

Length Index.	
Internes and Patients at Garrison Hospital .	89·0
Enlisted Men	87·3
40 Tuberculous Chests (Buffalo)	80·0
40 " " (Brompton)	81·4
Abnormal Chests.	
Prominent.	Breadth Index.
Fœtus at Term (Fœtal Rickets)	159·0
Girl æt. 18 yrs. (Rachitic Dwarf, height 2ft. 11in.)	152·4
Man æt. 20 yrs. (Dorsal Kyphosis)	143·0
Flattened.	
Man æt. 23 yrs., Funnel Chest ("*Trichter-Brust*")	54·0
Flattest Chest of Normal Series (Soldier, 31 yrs.)	61·0
" " Tubercular " (Male, 38 yrs.)	66·0

On account of the diminution of the transverse diameter, the tubercular chest looks longer than it really is, and our eyes have only misled us here, in the direction of over estimation. The meaning of this departure is quite obscure. As although the quadrupedal chest in nearly all forms is distinctly longer than our own, and the reptilian, and piscine still more so, and there are traces in the human embryo of at least two pairs of lumbar, and one pair of cervical ribs, which have been suppressed, yet the chest in the infant is short in proportion to its breadth. But, it is certainly long in proportion to the stature, although I can find no measurements giving the exact proportions.

To sum up, the tubercular chest is not only relatively, but absolutely "deeper," narrower, and longer than the normal.

Instead of being flat it is round and long, or, as it has been termed with grim appropriateness, "coffin-shaped." In all of these dimensions, it is apparently a chest arrested at a certain stage of its development.

I was much interested to learn a short time ago, in the course of my later measurements, from Dr. Felkin, the Resident Physician at the Brompton Hospital, that some years before, Mr. R. J. Godlee had expressed a similar opinion as to the real shape of the tubercular chest, and that his own observations since had confirmed the opinion. Which, in view of the enormous number of cases passing under his care, I regard as most weighty evidence in corroboration.

The practical bearings of these observations are of obvious importance. If an arrest of the chest-form at about the period of puberty is a predisposing factor in tuberculosis, then we have an indication of the pre-tubercular state, of easy application, and of no little value. Of course, by no means every chest with a Breadth Index of 80, or over, becomes tuberculous, nor do all chests reaching 71, or less, escape, but in view of the facts that among fifty soldiers only ten reached, or exceeded this tubercular average of 80 degrees, and among eighty-two consumptives only nine reached the normal Index, the persistence of the pubertal Index of 80 degrees would certainly be a condition to be regarded with suspicion, and got rid of if possible.

As for the cure, a vigorous active life in the open air, with plenty of tree climbing, ball—or spear—throwing, bar work, and all kinds of exercises which develop the great pectoral muscles, to pull the chest into shape, will be most effective. It would almost seem as if a reversion to the arboreal habits of our ancestors was the chief requisite for proper chest development in the individual, as well as in the race. The well-marked child-instinct for tree climbing ought to be regarded with respect in both girls and boys, even at the risk of torn clothing, or an occasional broken bone. Follow this by the weapon-throwing exercises of our less remote ancestors, for which, again, there is a sufficiently well-defined instinct in boys, at least, and a minimum of school or factory confinement, and we shall have far fewer "flat-chested," round-shouldered boys and girls growing up to become culture media for the tubercle bacillus. Tree climbing and war have *made* the human chest, and the magnificent instinct of the "natural man" and child for both, like most other human instincts, in Browning's phrase, "means intensely, and means good."

Now as to the other changes in chest-form or deformities proper—is there any ancestral basis for them? As has been seen by the measurements, there is a steady progressive modification of the nearly circular or barrel-shaped chest at birth, up to the transversely-oval chest of adult life. The question arises, is this transformation always complete? In my personal opinion it is not, by any means; and by the arrest of this progress at some particular stage, and exaggeration by the processes of respiration of the proportions which are normal at this particular time, the majority of the deformities of the chest are produced.

Let us take, first of all, the condition of "pigeon breast." None of the current theories attempt to shed any light on the crucial question of the whole situation, viz., why a chest which is normally widest in its transverse diameter should suddenly begin to flatten in this diameter and increase in the opposite one. When, however, we look at the question in the light of this change of shape, which is taking place, then we at once see that pigeon breast is simply persistence or mechanical exaggeration of the normal, ancestral, and fœtal, antero-posterior or "keeled" chest. The change or deformity usually begins during the first six to eighteen months of infant life, when the chest is, in the normal child, of nearly equal diameters, and hence capable of elongating with equal ease in either one of them, if pressure is brought to bear on it in that direction. In some cases, however, it begins later, when the chest has begun to assume more nearly its adult form, and in this case we have not only a mechanical cause to consider, but also the question whether we have not what might be termed a line of least resistance, which is here, as everywhere, in the direction of the ancestral type.

But supposing we have, as is usually the case, a chest whose diameters are nearly equal, or even with the transverse slightly in excess (although it must be remembered that in children who are subjects of pigeon breast there is usually a general backwardness of development in the formation of the skeleton, and that in many cases we have actually a persistence of fœtal type after birth, so that the antero-posterior diameter is excessive to begin with), what influence is there which will cause the drawing together of the lateral walls and the forward protrusion of the sternum? In the first place, a small amount of influence in this regard may be exercised by the so-called accessory muscles of respiration, the sternal group, all of which tend to pull the sternum upward and slightly forward. But the influence of these is comparatively slight in normal respiration, and would probably be more than overbalanced by the opposite tendency on the part of the intercostals, which are weaker and thinner toward the sternal end of the interspaces, and lacking over the region of the sternum.

There is, indeed, one factor alone which we believe is adequate to account for this singular distortion, and that is the great muscle-sheet of the diaphragm. This fan-shaped sheet curves up over the roof of the abdominal cavity in a high vaulted dome, which dome, by the contraction, particularly of the great crura, is sharply flattened and pulled down, and also flattened from side to side by the lateral fibres; the vertebral column and the inner surface of the lower ribs acting respectively as fixed points in this descent. That the diaphragm is chiefly concerned in the production of this deformity is admitted by all, and a variety of explanations have been offered to account for its excessive and extraordinary action, chiefly in the direction of obstructions to the entrance of air into the chest, in the form of enlarged tonsils, adenoids in the pharynx or obstructions in the nasal passages. None of these, however, can seriously interfere with the current of air entering the lungs, for the simple reason, that they can all be "short-circuited" by breathing through the mouth. And this soon becomes the habit in children. The real interference with its action is at the other end of the scale, and comes not from above but from below. Normally the diaphragm uses the ribs and vertebral column as its fixed points and pulls down the arch of its centre, but when the vault of this centre is firmly supported and fixed by a mass of abdominal contents, distended by gas, engorged by portal blood or packed with enlarged lymphatics, then the action of the muscle is reversed as to its lateral wings and the centre becomes the fixed point and the ribs the point acted on.

In other words, given a swollen, œdematous, abdominal mass, and you have the diaphragm at every respiration pulling the lateral chest walls inward and upward, instead of using them as a fixed point to pull its centre downward and forward; and this swollen abdomen, which in its extreme form gives rise to the familiar "pot-belly" of poorly-nourished children, is precisely the condition of affairs which we find in the majority of cases of pigeon breast. Since I first became convinced, some seven years ago, that pigeon breast was thus produced, I have carefully noted this condition in all that I have been able to see, and have never yet found a recent case in which the abdomen was not distinctly enlarged. Pigeon-breast is a thoracic defect of abdominal origin. This pressure is exercised almost solely in the transverse direction for the reason that between the vaulted centre and the sternum there are no muscular fibres, but only the central tendon, while the muscular masses running from the central to the vertebral column slope downward so rapidly as to cause a protrusion of the abdomen instead of a sinking of the sternum. This explanation will also account for the frequent association of this condition with struma and rickets, in both of which this swollen and distended condition of the abdomen is extremely apt to occur, while in the latter there is also an abnormal softness of the bones rendering them still more liable to distortion.

Will this relation of affairs account for any other of these conditions? For instance, the well-known but not so common "hour-glass chest" with its *Harrison's groove*, as it is termed. At first sight it would not appear to do so, for the situation of the groove is somewhat peculiar, not at the level of the costal attachment of the diaphragm, but about two interspaces above; in fact, from one to two interspaces below the nipple. First of all, however, let us observe that this groove or constriction is not so much a diminution of the diameter of the chest above this point, as it is a line at which the chest wall suddenly begins to flare outward, and that we are really dealing with a chest of fairly uniform calibre down to this point, but of a sudden and marked widening beyond it. In a few cases, however, the constriction is not merely relative, but absolute as well. As I said, the situation of the groove at first view does not appear to fit in with our theory; but if we will examine a little more closely what the direction of the tension of the normal diaphragm is, we shall be able to give some explanation of how it is produced. The pull of the diaphragm on the lower ribs, when its centre is fixed, is not directly inward but inward and upward. Now what will be the result of traction in these directions acting on a yielding and movable framework, like the walls of the chest? Obviously, that the lower ribs having but little or distant attachment to the sternum, would be glided upward and inward *en masse*, until they meet the resistance of the more firmly attached sternal or true ribs above them. When this takes place, their further progress will be abruptly stopped, and the pull still continuing they will, as it were, rotate round this fixed point of the sixth or seventh interspace as upon an axis, and instead of sliding upward and inward, begin to flare outward, assisted by the pressure of the swollen abdomen below. Consequently, we would expect to find Harrison's groove occurring in children, in whom this marked abdominal distension did not develop until after some degree of rigidity and some approach to the adult form, had begun to be attained by the chest, and this will be found to fit with the clinical facts of the case. When once the "flare" has begun, it will be exaggerated both by the pressure of the distended abdomen below, and also by the tension of the intercostals, and to some extent by the lower fibres of the pectorals and serrati above.

In that rare and extraordinary condition known as "funnel chest," the "*Trichter-Brust*" of the Germans, we have a condition in which the lower end of the sternum in general, and the base of the ensiform in particular, form the bottom of a deep funnel-shaped depression, around which the thoracic walls bulge out above and the abdominal walls below. This is a much more complicated state of affairs, and, in the light of our present knowledge, difficult of explanation; but we believe that the principal factor will be found to be a firm binding down and back of this portion of the sternum, which is accordingly prevented from yielding in the antero-posterior direction, while the walls of the chest above it and at the sides are advancing in normal growth or bulging under the pressure of the wings of the diaphragm. In other words, I believe it to be, if we may use the expression, a pigeon-breast in which the lower end of the sternum has been firmly bound down and prevented from yielding and growing in harmony with the rest of the chest wall.

The same explanation will also apply, and much more obviously, to the condition of "guttered" sternum. Here we have a chest which upon measurement will be found to be distinctly above the normal in its antero-posterior diameter, but in which the greatest projection is not in the median line, but in a line drawn parallel with it upon each side about two inches from it. When we examine what that line represents, we find that it corresponds to the sternal ends of the costal cartilages, and is paralleled by a groove corresponding to the costal ends, the weakest and most yielding point in the entire chest wall of the child. We have here simply a pigeon-breast, in which sufficient tension is exercised by the central tendon of the diaphragm upon the lower end of the sternum, to prevent that bone from moving forward freely *en masse*, and consequently the lateral tension of the diaphragm is expended upon the line of least resistance, which happens to be a double one, and corresponds to the sternal end of the costal cartilages. The curious one-sided bulgings of this description may also be explained in the same way, on the ground that the nutrition of the costal cartilages on the one side was inferior to that of the other. Again the importance of rickets as a predisposing cause of this disease is self-evident.

Deformities of the quadrupedal chest are much rarer than those of the human thorax, for the simple reason that the mechanical strain upon its walls is so much less. Exaggerations of the vertically oval form of the chest occasionally occur, especially in rickets, corresponding to our pigeon-breast, but these are much less striking, and it is harder to draw the line between them and the normal shape.

In our semi-erect kindred the monkeys and apes, however, a readily recognizable pigeon-breast is quite common. So extreme indeed becomes the projection of the sternum and flattening of the sides of the chest, that these latter are often found actually collapsed after death. The lateral walls of the chest are almost in contact with each other *behind* (dorsal) the pericardial sac. The lungs are collapsed, and there is usually no other discoverable cause of death, though the bones are softened and rickety. My own first impression was that the monkeys had been crushed and smothered in the press, as they huddled together in the cold nights, and their softened ribs crushed in. But Mr. Bland Sutton informs me that he had frequently noted the same condition in his autopsies, and regarded it as due to collapse of the chest after a violent fit of coughing, with expulsion of the residual air. Whatever its cause, it is not at all an uncommon *post-mortem* condition among them.

I have also found two cases of Harrison's groove in monkeys.

CHAPTER VI.

The Diseases of the Heart and Bloodvessels.

Probably in no class of the divisions of our citizen-cells are the variations, between the individual workers, wider, in range than in this great group of the circulating or transportation-system of the body. From the free, roving and independent leucocyte, to the fixed and almost devitalized fibrous or elastic cell of the aortic wall, or of the heart-valve, is so wide a step that at first sight we can hardly believe that both belong to the same class and family. And yet there is nothing which the later developments, both of biology and of pathology, have ever demonstrated with more absolute certainty. The heart, the vessels and their contained blood are to be regarded as one great continuous tissue-tree. We have, of course, long passed the idea that the bloodvessels of the body simply "contain" the blood in the mechanical manner that a gas-pipe does the current of gas; but we are still, to my mind, far from appreciating, either the essential and high degree of vitality of every part of the vascular walls, or, what is more important even, the immediate genetic relation between these and the plasma, and corpuscles which they contain.

A glance at the vascular area in any mammalian embryo will give us most suggestive light upon this point. There the bloodvessels are to be found forming, not only by a process of budding or ingrowth from vessels already formed, after the manner of a tubing or a drive-well, but also by a simple gaping, as it were, of spaces between the cells, which are promptly walled in by the living units along their sides; or even, in some cases, one of these living units will prolong itself and appear to hollow out a space in its own interior to contain the vital fluid. Connections are gradually opened up, either by end-to-end absorption of the individual cell walls, or by a crevasse-like opening of these apparently fortuitous interspaces, one into the other, the pulsations of the heart-current begin to find their way into these ditches in the vein-swamp, they become hollowed out and definite, their walls begin to thicken, and behold, we have a network of fully formed bloodvessels showing in every direction through the formerly spongy area.

And what is the origin of the contents of these tubes? In the first place, they are filled simply by the more watery elements of the soft and jelly-like protoplasmic tissue, and the process is apparently almost as simple as that by which the whey is separated from the curd in the coagulation of milk. In a very short time, however, individual cells appear, floating free in this watery medium, and we soon discover that these are being simply budded off from the inner surface of the living cells which wall in the space or tube.

Thus, the bloodvessels and their contents are emphatically one continuous and homogeneous tissue. The fact that this tissue happens to be fluid in its centre in no way destroys the vital relations and continuity between the two parts. To use our tree-simile again, if we could imagine that in the process of growth of, say an elderberry stem, after the outer wall had hardened into its familiar woody casing, the pith in the centre should liquefy and send its suspended cells floating down the current, we should then have a rough, but almost absolutely analogous, representation of the process of blood and vein-building in our own bodies.

And is it any wonder that we should still find in adult life, not merely in health, but also in disease—notably in the so-called processes of repair and inflammation—that this same primeval sympathy, this literal "tie of blood," should be found to play an important part in controlling the behaviour of both tissues? For instance, in the classic four steps of inflammation, remembering that the walls of the vessels are simply a part and parcel of the tissues in which they lie, indeed, that from the fixed tissues outside through to the vascular wall, and from the vascular wall through the endothelium to the leucocytes, is really one continuous tissue, is it any wonder that the first threatening of danger, much more direct injury to any part of the fixed tissues, even though the vessel wall itself be not involved, is instantly responded to. First upon the part of the vessel wall, by dilating and inviting larger volumes of blood to flow into it, and secondly upon the part of the leucocytes, by instantly responding to the signal of the endothelium, and anchoring themselves to the latter, prepared for any emergency. In fact, it seems to me that those extraordinary changes, so intelligent and so vitally important, which we group together under the term of "stasis" are practically utterly incapable of adequate explanation, not merely upon any mechanical ground, but upon anything less than a full recognition of this vital sympathy, and direct connection between all three of these divisions of the great binding-stuff group.

And the same factor must be admitted in the further development of the same process, particularly in any extraordinary emigration of the leucocytes through a vessel wall, which ten minutes before was apparently as impervious to them, or at least as unattractive, as if it had been made of rubber or glass. Indeed, we very much doubt, as Wesley Mills has so aptly suggested, whether it is any longer possible to regard or attempt to account for the simple escape of serum or plasma through these walls upon osmosis or any other purely mechanical principle. Certainly the slight change in the pressure in an inflamed area is absurdly inadequate to account for the extraordinary increase of this transudation process. Not only this, but, as he has well pointed out, although very little is known of the so-called "lymph" or tissue-fluids of the body (and yet here is the vital and important place, where any changes in the composition of the blood or lymph are producing their beneficial or deadly effects), such investigations as we have been able to make, have shown a marked difference between the normal lymph or tissue-serum and that which is poured out in inflammation; and between this latter and the so-called lymph saturation of œdema or dropsy there is, again, a wide and striking chemical difference.

In other words, we are decidedly inclined to agree with the bold conception of the above observer, when he declares that the capillaries are to be regarded as *glands of local origin*, and that the fluids which pass through their walls are not merely transuded or filtered through them, but are actually secreted into the tissues by the capillary endothelium; and that this secretion varies not only according to the condition and composition of the blood, but also with the condition and needs of the tissues in their particular region.

In the present state of our knowledge, of course, we are not prepared to go beyond the tentative stage in this proposition; bnt it does seem to us that it affords a more adequate and rational explanation of many of the phenomena of the capillary transudation in both health and disease than any other which has, as yet, been suggested. Take, for instance, those singular dyscrasiæ, in which there is a marked tendency to the escape of the red corpuscles in certain definite situations, the whole group of the purpuras and the old "spotted fever," the "black" form of small-pox, and many other similar conditions. Here, mere chemical changes in the blood, in the vessel-wall, or in the tissues, separately considered, are inadequate to account for the singular distribution of the phenomena; but, let us regard these as practically all one tissue, so that any toxic effect upon the fixed tissues, or nutritive effect through the nerve-supply may be promptly transmitted to the capillary wall, and through that to the blood. Then instead of the serum alone being secreted and the white corpuscles attracted to pass through the openings, formed by the contraction of the endothelial cells, the red blood-cells are destroyed, apparently by contact with the diseased vessel wall, and their broken-down remains promptly excreted by the same, to prevent their blocking the current or poisoning the entire blood-stream.

The frequent association of these disturbances with hæmorrhages from the mucous membrane, and from the tubules of the kidney, would also coincide quite closely with this possible method of its production; and when we come to those still graver and more utterly mysterious disturbances, known as icterus of the newly-born, melæna, etc., it is impossible to resist the conviction that in the blood-vessels and fixed cells we have one continuous tissue, by the disturbance of the delicate relations between which, the normal *entente* between the middle and central divisions of the tissue, the blood and its retaining wall, may be so completely destroyed, that it is, so to speak, a matter of indifference to the latter on which side of it the red corpuscles move. And there appears to be a distinct element, of this disturbed balance, in the all-too-familiar and dreaded hæmoptysis of the early stages of pulmonary tuberculosis. About all that we can say of it, is that in eight cases out of ten it is not due to any ulcerative process involving the vessel-wall (in fact, it usually occurs long before any such stage of the process has been reached), but that, in some way or another, the capillary walls, of one of the most vascular, and by far the most unstable organ of the entire body, lose their power of retaining the red corpuscles. This, of course, applies only to the preliminary hæmoptysis, and not to the often serious, later hæmorrhages, of erosive origin, in this disease.

And I cannot help thinking, that in that extraordinary, to say the least, coincidental relation between anæmia and puberty we have, again, an expression of sympathy between two descendants of the great mesoblastic group, the blood and the vascular tissues, upon the one hand, and the uterine, muscular, osseous and general connective-tissue changes, which occur at such a high rate of speed at this particular period, upon the other. I am aware, of course, that this time coincidence may often be explained, as has been suggested and almost demonstrated by Glenard, Stockton and others, by making the anæmia due to an intestinal toxæmia from enteroptosis, caused by the deadly corset habit, which is usually first established about this time. But I think that we have also to deal with a developmental tendency in this direction, at this period, which the toxæmia, important as the part unquestionably is, which it plays, simply acts upon and intensifies.

So far we have been dealing only with the fluid core of the vascular system, the blood; but, of course, in the adult body we find that the vessels and their walls have undergone some very extensive and divergent specializations. So long as all the tissue-web retained its powers of contraction, and by frequent exercise of them the blood could be churned around, as it were, in haphazard sort of fashion, through these irregularly branching and frequently communicating interspaces, there was no need of anything more than a mere retaining wall for the channels. But with the growth of the body-mass, and the specialization of the fixed tissues, a further development becomes necessary, and this takes place in embryo by the appearance, as the surrounding tissues lose their freedom and abundant power of contraction, of a distinct contractile element, the so-called muscular coat. At first this is distributed with fair uniformity among all the larger vessels, and is the common property of the entire vascular tree; but at a very early stage some further specialization in the localization of this contractile and propulsive power is found necessary, and (according to the organism) a heart or hearts spring into being. This organ is nothing more than a single, bulb-like pouching or enlargement of a certain limited area of the general vascular tree. Originally the walls were thickened, but very slightly—simply the ordinary amount of muscular coat possessed by the rest of the vessels being present; but a step further on in the division of labour, this begins to rapidly thicken and increase, while that in the vessels remains at a standstill, until ultimately we come to the development of a sac of six or seven times the diameter of any other part of the blood stream, and with an enormously thickened and powerful wall, composed almost exclusively of muscular tissue. There is absolutely nothing in the heart which cannot be found in any part of the venous or arterial system—it is only the proportional development that is changed; and its relation to the arterial system is merely that of the bulb of a

Davidson syringe to the tubing. And this, although an individual history in the embryo, is of course, as everywhere, an epitome (whose sequence is altered in some respects) of the long line of ancestral changes which, in the remote history of the raçe, have led up to this superb piece of mechanism.

The first "heart" of which we have any record is that singular gap in the protoplasm of the amœba, known as the "contractile vacuole," and it is the foreshadowing of the intimate relation which is to exist, even in the higher stages, between the bloodvessels and the excretory mechanisms, that authorities differ as to whether this vacuole is really a circulatory or an excretory "organ," the probability being that in this low stage of the development it serves both functions. Its method of formation appears to be, if we could imagine such a thing, an agreement upon the part of some area of the protoplasm to contract or to flow away from a certain point, thus producing an area of lowered pressure. Into this the more fluid contents of the protoplasm promptly flow, and with them probably some of the excretory products of the tissue. When the vacuole has grown to a certain size, the protoplasmic ring around it suddenly reverses its action, contracts sharply back upon itself, and squeezes the contents in both directions into the surrounding tissues: or, as seems very possible, this contraction is sufficiently purposeful to drive the contained fluid out toward the periphery of the mass, where it may be got rid of. A process of which the capillary formation by vacuolation in the vascular area of the human embryo, is a singularly accurate imitation.

In the hydra we get distinct and very rapid currents flowing in different lines and directions through apparently either much more liquid tracts or actual vacant spaces in the protoplasm, but, as yet, no distinct vessel wall.

In worms we find the vessel wall developed, and everything in readiness for the next step. The vascular system simply consists of a pair of longitudinal vessels running the entire length of the body, which, subdividing at the ends, open into the tissue spaces. At about the junction of the anterior with the middle third of these tubes, a little bulbous enlargement appears, and in some forms two, or even three, of these bodies will appear in succession upon the short transverse trunks connecting the dorsal and ventral "aortæ." When they have attained sufficient size, the slow and irregular contractions of their muscular coat become transformed into distinct and powerful pulsations, and a steady current of blood is driven through them, or, more accurately, probably, from them, in both directions—much the same process which is seen in the appearance of the so-called "heart-tubes" in the embryo, and their bulging and finally uniting with each other to form the primary heart cavities. And the pulsation is by no means unique, for, as the recent researches of Starling* have shown, a similar rhythm is present in the muscular coat of the vertebrate intestine.

It must not be supposed, however, that we are here dealing with a clean and absolute cavity in these bulbs; the condition is more primitive than this, and is most strikingly and interestingly illustrated in the heart of the mollusc, which has no distinct central cavity, but is simply an enlarged colourless, pulsating sponge, into the interstices of which the fluids of the body are sucked in its expansion, and propelled out of them by its contraction. It was not even necessary for the tissue to completely hollow itself out, so to speak; in fact, the vigour of its contraction would probably be improved by allowing strands of contractile fibre to pass from one side of the bulb

* *Journal of Physiology*, May 11th, 1899.

to the other, through its central cavity, and, curiously enough, we have a distinct trace of this stage of development, in the adult human heart, in the elaborate network of muscular fibres which line its inner wall. We would certainly have thought that here a perfectly smooth and unbroken surface would have been a distinct advantage, such as we find in the larger arteries, for instance; but, instead of this we find a most elaborate structure of projecting, and in some cases, even, independent muscular bands, the *columnæ carneæ*, attached along their sides or simply at both ends to the walls of the heart. In the *musculi papillares* we have a few of these which have retained even more of their ancestral position and run from the wall of the heart to another part of its wall which has been transformed into the valve; while in the hearts of some of the higher mammals, notably the ox, we find a local persistence of the molluscan condition in the band or bands which run directly across the ventricle from one wall to the other, the so-called "moderator band."

In some of the higher Worm- and in Molluscan hearts, still another development puts in an appearance. Little folds of the tissues lining the cavity project flap-wise across its orifices, and valves are produced, and a definite course given to the stream. But in the lower orders their activity is of an apparently haphazard sort, often alternating, and their effect is mainly to keep up some sort of movement, in any direction which may happen to be convenient, of the vital fluids. In the Fish-heart we find a well developed cavity with valves and thick wall, and also a division of its lumen into two compartments, an earlier or "venous," and a later "arterial" bulb; and the auricle and ventricle are born, the former, however, distinctly the earlier of the two. In the Amphibia a still higher development occurs in the dividing of the auricle, while the ventricle remains single. In the Snakes this same condition persists in the lower forms, while in the higher the ventricle also partially divides, and we get the four-chambered heart, which is typical in Birds and Mammals.

From start to finish the ancestral process has simply been a question of local specialization. The endocardium is, of course, identical with the endothelium of the most primitive capillary or the lining cells of the worm's pulsating tube. The muscle of the heart-wall is an almost absolutely identical structure, from the heart of the worm to that of the highest mammal, and from the tiniest arteriole to the left ventricle.

Nor is this process of specialization necessarily limited to any one region of the vascular tree. In the worm, as we have already seen, there may be from three to six pairs of these pulsating bulbs in succession; in some of the amphibia we find as many as six and even eight "hearts" (Salamandra), not confined to the blood vascular system, but also concerning themselves with the propulsion of the lymph. The frog, for instance, has four of these slowly pulsating lymph-hearts—two in the axillary and two in the sacral region—these latter persisting also in many other forms, and surviving in even the human body in that almost functionless and most feebly-pulsating sac, the *receptaculum chyli*, a structure whose spongy size is well-nigh useless, if it be not the remains of some more active and effective mechanism in earlier stages. And the *retia mirabilia* which are found upon the carotid of the horse, the intercostals of the whale, the mesenteric vessels of man, probably even the spleen itself, may possibly be originally of this class of structure.

When we come to look at the localization of disease throughout this extensive tract we shall, I think, find that the law already developed, in the chapter upon diseases of the lung, of close relation between biologic recentness and pathologic instability, will be still seen to hold. The one part of the vascular system, which appears latest and has progressed farthest away from the normal protoplasmic type, is that tissue which of all others appears to be toughest and most resisting and least in danger of suffering in its nutrition, the firm, fibrous leaflets which form the valves of the heart and their connecting tendons. But, if we were to be asked to put our finger upon the weakest spot in the entire circulatory system, all experience would justify us in placing it on these tough, leathery-looking little flaps.

Some of this "bad eminence" is of course due to the vitally important changes, which may be produced by the destruction of a very small amount of tissue at this point. But then nature would appear to have compensated for that in advance, as far as might be, by their conversion into such a firm, tendinous, whipcord-like material. Much also of their peculiar liability to disease is obviously due to the tremendous pressure under which they work, and that they are the point of by far the most violent alternations of tension in the whole system. And yet this would hardly account for their extraordinary liability to become the seat of vegetative growths in the various infective forms of endocarditis. In fact, upon purely mechanical grounds they would seem to be one of the last places in the whole blood stream upon which micro-organisms could succeed in getting a foothold. Moreover, if this purely mechanical wear and tear were the chief cause of their diseases, we should expect to find that their defect would most frequently be that of insufficiency, just like a leaky valve elsewhere, either by the stretching of the chordæ tendineæ or the sagging or thinning of the edges of the flaps themselves.

But, as every clinician knows, this is the least common form of valvular defect, and we doubt if more than a very small proportion of the cases in which insufficiency is present can be traced to any such method of production, the defect being usually due to loss of substance or deformity, following some form of inflammatory or infectious disease. Of course, by far the most frequent defect is stenosis, due to a matting together of the flaps and narrowing of the orifice, by cicatricial contraction following some inflammatory process. Liability to this form of attack is not a pathologic monopoly of the valves alone. An endarteritis or phlebitis from septic or other causes is one of the commonest disturbances throughout the entire vascular system. But, for some reason or other, the valves of the heart appear to be possessed of less power of repair and fewer possibilities of recovery than the other parts of the system, and we think we are justified in regarding a considerable share at least of this lessened recuperative power, as due to the fact of their wide departure from the primitive type. Their tissue has become so nearly devitalized that apparently, it is both more liable to the attack of the invading infections and less capable of repairing their ravages than any other part of the system.

And it is hardly necessary to remind you, first, that the valves are the last part of the mechanism of the circulation to appear in our ancestral tree, and also in our embryonic development; secondly, that they were originally a muscular ring of sphincter-like character, projecting from the heart-mill; and that in birds and reptiles their flaps still contain muscular fibre. In the very earliest molluscan heart, the valve is little more than a thickening of the circular muscular layer and a slight corresponding projection of the lining layer, such as we find at the pylorus in the human species. The valves above, the *chordæ tendineæ* in the middle and the *musculi papillares* below, are all simply the modified parts of a former muscular ring which projected into the lumen of the orifice, and closed it sphincter fashion. Of course, this thick and clumsy arrangement was quite inadequate to the necessities of mammalian circulation, although it is a curious fact that distinct traces of it still remain in that class where some of the most brilliant and rapid circulatory work that can be found anywhere is demanded of the organ—in the bird family—whose right auriculo-ventricular ("Tricuspid") valve is still a spiral fold of muscle. And although our knowledge here is extremely inadequate, yet so far as it goes, in spite of the tremendous strain put upon the heart of birds, valvular or cardiac lesions upon this side of the heart are rare, if not almost unknown, among them. And when this degraded descendant of the muscle-cell in the mammalian heart is destroyed or damaged, the only thing it can fill the gap with is the lowest form of really living tissue, the fibroid; and this, by its fatal after-tendency to contract, often widens the rent which it was intended to repair. In short, here, as everywhere in the vascular system, contractile power equals safety, loss of contractile power—danger, either immediate or remote; and as long as the heart-muscle retains its ancestral power of reproduction and contraction, which it does up to the very last moment that nutrition is supplied to it, so long may a balance be maintained, and life almost indefinitely prolonged. I need hardly point out that this dependence of vigour and safety upon contractile powers, holds good throughout the entire arterial system. The substitution of fibrous, and later of calcareous tissue, for the muscular coat of the arterioles, whether in the kidney, the brain, or the liver, is the very key-note of that foundation factor in all sorts of chronic disturbances, arterio-capillary fibrosis—the commonest simple structural cause of disease in the adult and senile body.

And this curious instability of the parts last developed is also shown in the functional disturbances of the organ. As Wesley Mills has brilliantly pointed out:—"Functional action ceases in the hearts of the cold-blooded animals invariably in a certain order, that is to say, the parts latest developed phylogenetically, the ventricles, are the first to cease to act; the same applies to the mammals. . . .

"Now, in the morbid human being there may be only an occasional beat of the ventricle to several of the other parts of the heart; or the ventricles may pulsate so feebly as to expel but little blood. Hence, the latter becomes gradually more venous, with corresponding effects in the venous channels, which become more prominent. A gradual loss of the functions of the cerebrum, a lowered temperature in the most distant parts develops, and, finally, the only muscles that remain functionally active are the respiratory, the sphincters, etc. In a word, the dying human subject sinks functionally lower and lower in the scale of animal life." *

I think there can be little doubt that some of those singularly arhythmic, dicrotic heart-movements which we get either in the last stages of valvular disease or before impending dissolution, are due to ventricular contractions ceasing to be synchronous with the auricular; and in one or two cases of neurotic arhythmia, I have been able to detect, at the base of the heart, an apparently steadier beat, more rapid than the ventricular. The part first developed—the auricle—retains its vitality the longest, and attempts by increased activity to compensate for the failure of the

* "Medical Record" (New York), October 22, 1887.

ventricle. And even in temporary conditions of depression, such as fainting and shock, this singular and single-handed persistence has several times been found to occur.

The part which has utterly lost the power of contraction is in the gravest danger, while those structures which come nearest to this "mummification," the purely fibro-elastic walls of the aorta, are the next points of least resistance, as shown by their peculiar liability to atheroma, calcification and aneurysm.

As the heart reaches its climax of specialization in the higher Reptiles, and from this onwards remains the most absolutely uniform and unvarying organ in the higher vertebrate body, we would naturally expect to find but few important differences between its disease-liabilities in different classes and orders. And the facts justify this expectation.

Diseases of the heart in animals are almost identical in character and causation with those of our own species. The only important difference being their lesser frequency, which is most marked in birds. Their precise frequency in animals is difficult to decide, for several reasons; the proportion of them ever examined in this respect is, of course, extremely small, as is also the percentage which are permitted to reach the age at which these lesions are most prevalent. Then, the physical difficulties in the way of its examination during life are very great, both on account of its central position in the chest in all diameters, and, consequently, almost complete enfolding by the lung, and from the thick layers of muscles which cover the small region, just behind the shoulder (elbow), where alone its apex approaches the ribs. In fact, it is only in the flattened human chest, where the lungs have fallen back on either side, that the heart comes to lie sufficiently forward and in contact with the chest wall, to permit of a really adequate examination. In the horse, ox and sheep, only the apex and a very small portion of the left ventricle are exposed, in the pig only an area about an inch across, in the dog, the heart touches the chest wall, along a part of the narrow sternum only, and in no other animal are the origins of great vessels accessible to examination at all. In the bird, the organ is completely surrounded on all sides by the lungs and air sacs.

As might have been expected, the statements of authorities differ as to the frequency of disease. Friedberger and Fröhner regard it as very common, Lubarsch and Ostertag as frequent, Law as moderately frequent, while Leblanc found heart lesions in 5 per cent. of 150 autopsies upon domestic animals. In wild animals and birds cardiac mischief is distinctly rare; as in 200 autopsies, in various zoological gardens, I have found valvular or endocardial lesions only six times; in the fifty birds, not a single case of grave cardiac lesion was discovered, the nearest approach being a small hard mass of uric acid deposit, at the base of the spiral valve in a vulture, and moderate atheroma of the ascending aorta in a parrot, although a mild form of pericarditis, with a small amount of milky or creamy effusion, was fairly common. A similar form of pericarditis was also present in four of twenty snakes examined, and in both of these classes I suspected the milky appearance to be due to the presence of urates, which, however, I was only able to detect in two of the cases, that is in birds.

Cardiac disease is decidedly commonest in those animals which have the largest hearts in proportion to the size of their bodies, such as the horse and dog, whose heart-weight is as 1 : 100; and rarest in sheep and cattle, both of whom have hearts of less than half the size, 1 : 225. As these first-mentioned animals are of course exposed to much greater heart-strain than the latter, it seems probable that the increased size of their hearts and their greater liability to disease are the result of the same factor.

The commonest and mildest form of abnormality, cardiac *hypertrophy*, has a distinct physiological basis. Indeed, as in our species, it is hard to say in some cases where the normal enlargement leaves off and the abnormal begins. It is most frequent in those breeds of horses and dogs in which the heart is normally the largest—racehorses and hunting-dogs. The ordinary weight of the horse's heart is from 5 lbs. to 9 lbs., and this in hypertrophy may be increased to 10 lbs., 14 lbs., and even in one case reported by Stevenson to 31 lbs.; and this last weight has been equalled in the ox (Herran). In the thoroughbred racehorse, however, the lower of these weights may be reached by a normal heart, that of the celebrated stallion Helenus weighing 14 lbs. As is now well recognized in the human athlete, the physiologically enlarged heart may become a source of danger, especially if its reduction to the normal is allowed to take place too suddenly. It is not the vigorous discipline of training that injures the heart, but the sudden relapse into the life of the office and of the loose-box respectively, which too often follows the end of college life in man, and of the racing season on the turf. The fatty and fibrous change by which the reduction is effected goes too far.

The causes which induce hypertrophy of the equine and canine heart are exactly the same as in our own species—overstrain, valvular mischief, obstructive diseases of the lung, adherent pericardium, contracted kidney.

And as in our own species, after the limit of compensation has been reached, then comes dilatation. This may occur to an enormous extent, as in a case in a hunter reported by Dyer*

* Quoted by Law.

in which the pulmonary orifice was dilated sufficiently to admit the closed fist. It is almost constant in advanced cases of "broken wind" (asthma), and quite common in overfed beef-cattle, owing to the obstructing effect of the enormous accumulation of fat around the base of the heart.

Next most common is *pericarditis*, which is usually of infectious origin, tubercular in cattle, rheumatic or septic in the horse, especially as a sequel of pneumonia. A unique form of the disease is the traumatic variety in the ox and goat, due to the penetration of sharp foreign bodies, baling wire, nails, needles, etc., from the great paunch and second stomach. Nearly every veterinary museum contains several specimens of this curious lesion, and in some cases the heart wall also is penetrated.

Pericarditis with effusion is quite common in most species of wild animals and birds in captivity. Nearly half the cases I have found were tubercular: two, one in a gazelle and the other in a kangaroo, were due to echinococcus cysts, and in two monkeys there were quite extensive adhesions.

Myocarditis is rare in animals, and when it does occur, it is usually of infectious origin; and the same is true of degenerative changes in the heart-wall generally, except such as follow hypertrophy and dilatation. Fatty infiltration occurs in overfed oxen, and a flabby, slightly fatty condition of the muscle is not uncommon in wild animals in captivity; but I have never seen it sufficiently extensive to give rise to œdema or other circulatory disturbances, or to affect the general system in any way.

Endocarditis is fairly common in the domesticated animals, especially in the horse, and is almost invariably of the infectious variety, either rheumatic or due to streptococcus invasion. It occurs also among the carnivora which die at the Zoological Gardens, either as a brick-red to maroon-red injection of the entire heart-lining, or as a mottled hæmorrhagic effusion into and under the membrane, as I have found it in a badger and in a hyena.

Such *valvular lesions*, as occur in animals, are nearly all the results of endocarditis, including papillary growths, ulcerations, fibrous coagula, etc. I have found only three instances in my autopsies at the Gardens, vegetations in two carnivora, and a hæmorrhagic infarct in the substance of an aortic valve in an elk. Like all other heart changes, they are much commonest in the horse and dog, in whom they occur more frequently, as in ourselves, upon the left side of the heart; in the ox, however, for some unknown reason, they are more frequent upon the right side.

Rupture of the heart is rare, and though it may be caused by a sudden violent strain, especially in old animals, yet is most commonly due to the lodgment of parasites either in the wall or within the cavities of the organ. *Filaria immitis* swarms in the blood of the dog, and may accumulate in such numbers in the heart cavities as to cause rupture of the wall, while a *Strongyle* or an *Echinococcus* may lodge in the heart-muscle of the horse, giving rise to an abscess or to aneurysm, which may lead to rupture.

The malformations of the heart are even less common than in man. Several cases of *ectopia cordis* in calves have been reported by Herring, and I have seen one case, in a young heifer, at the hospital of the Veterinary Department of the University of Pennsylvania. The heart lay in the dewlap or brisket, completely outside of the chest, and could be grasped between the hands, and its pulsations felt with most startling distinctness.

I have only found one case of persistent *foramen ovale* in a wild animal. This was in a young giraffe, which lived to the age of about nine months and died of general œdema, affecting the lungs, pleura, subperitoneal tissue, and even the walls of the stomach.

Arteritis is comparatively rare in animals, except those forms due to the presence of hæmatozoa (*Filaria*, *Strongylus*) which, as we have seen in a former chapter, are extremely common in horses and dogs. When it occurs, it is usually of infective origin, and chronic senile atheroma, or arterio-sclerosis are seldom met with, though, doubtless, they are often overlooked. Only two cases of atheroma have occurred in my autopsies, one in the aorta of a parrot, and the other occurring as large, thick, calcareous plates in the aorta of an ox. This last condition is fairly common in the abdominal aorta of old horses.

CHAPTER VII.

Disturbances of "the Skin-heart" and of the Blood.

There is absolutely no *a priori* reason why we should believe that it is in the heart-wall alone, that the retention of contractile power is of such immense vital importance, and yet most of our text-books upon physiology speak as if it were the only factor in the motive forces of the circulatory system which was to be taken into account.

In tracing the pedigree of our mammalian vascular system, from its earliest ancestral form, as well as through its embryonic stages, we have solely to deal with the familiar process of division of labour and centralization of power. Beginning originally with the network of irregular "chinks" between the cells, which become walled by a simple, flattened, protoplasmic tissue, and this, as the surrounding cells lose to some degree their powers of contraction, developing into circular bands of muscle cells, each ring of which drives the blood onward, vermicular fashion, we find this universal contractile power gradually concentrating itself in one or more regions, with the result of the formation of a heart, or hearts, in these localities.

So that, finally, in the mammalian circulation we have the result of one large, thick-walled dilatation of the original tube, known as the heart, guarded by an elaborate series of valves, propelling the blood through an apparently comparatively passive system of blood tubes. We say "apparently" passive, because even the briefest study reveals the fact that these tubes are highly elastic, and to a degree which could only be possessed by living tissues, and that this elasticity plays a most important part in the circulatory mechanism. Secondly, that the calibre of the arteries and arterioles, particularly the latter, varies very considerably from time to time, so as to markedly influence the flow of blood to the part supplied by them. The mechanical reactions are obviously carried out by the presence of the elastic coat which forms the chief bulk of the wall in the aorta, and gradually diminishes in importance down to the arterioles; and the changes of calibre are equally obviously brought about by the vital contraction, or relaxation of the firm and powerful muscular wall which extends from the largest arteries down to the mouths of the very capillaries themselves.

This much of actual vital contractility is unanimously granted by all physiologists to the muscular cells of the arterial walls; but here their power apparently abruptly stops. And, while fully realizing that we are in a position to little more than raise the question, we wish to emphatically challenge this position, and assert not only the possibility, but also an apparent high probability, that these muscle-cells are possessed of far wider powers than those with which they are usually credited. In the first place, no one questions the fact that they are as thoroughly alive, responsive and capable of vigorous action as any other unstriped muscle-cell in the body, and it, certainly, is against all the analogies of what we know of muscular action everywhere else, that they should be capable only of such mechanical changes as will merely regulate the calibre of the tubes which they surround. We know of absolutely no form of muscle which is capable of that form of sustained and uniform contraction. Everywhere else muscular action is rhythmical, very slowly so in some cases, it is true, but still emphatically rhythmical; and only in a few tetanic, spasmodic conditions is it capable of maintaining a uniform contraction-level for more than a very brief period of time.

And yet this theory presupposes the extraordinary power, on the part of the muscular cells, of coming to a given point and retaining their contraction practically unchanged, not only for hours, but for days, and even weeks. The position becomes still more untenable upon *a priori* grounds when we remember the extraordinarily active part which is played by this very same muscular wall throughout the entire circulatory system of the higher invertebrates and the lower vertebrates, and that the heart is nothing whatever but a simple, localized aggregation of these very same muscular fibres. That this heart-forming tendency is not limited to any one locality, but may occur in two, four, six, or even eight different places in the body, that we still have, even in some of the highest mammals, those singular pulsating, spongy networks known as *retia mirabilia*, such as are found upon the collateral branches of the carotids in the horse, and which appear to act as local balance-wheels of the circulation. It would also seem not improbable that our own elastic, muscular, and highly pulsatile spleen performs some such pressure-regulating function for the portal circulation.

In fact, we cannot resist the conviction that this extraordinarily universal and vigorous muscle-coat in our arteries and veins has a higher vital function than merely that of mechanically narrowing the calibres of the vessels. As Wesley Mills aptly expresses it, "An inherent tendency to rhythmic contraction, all through the vascular system, including the vessels, must be taken into account." *

While this dissatisfaction with the usually accepted view of human physiologists was manifesting itself at the comparative end of the line, upon the extreme opposite wing of the army of medical progress, among the clinicians and the therapeutists, a similar though less articulate feeling was developing itself. We have long been conscious of the utter inadequacy of most of the explanations of the extraordinary tonic and beneficial effects of bathing, or splashing the surface of the body, with cold water. The familiar "reaction" theory has been growing more threadbare every year; for, if it simply consists in throwing more work upon an already exhausted or overloaded central organ, its ultimate effect would necessarily be similar to that of our boyish attempts to lift ourselves by our boot-straps. Not that this element does not play some part in the result, but that it is utterly inadequate to account for the general glow of satisfaction, the feeling of comfort and permanently tonic effect which is brought about by this simple but wonderfully

* "Animal Physiology."

effective means. Why the blood should remain for not merely minutes, but even hours, in the superficial vessels, with less effort on the part of the heart than before the plunge or splashing is, of course, hardly to be accounted for simply by any tonic effect upon the heart or central nervous system; but when this remedy began to be systematically applied in therapeutics, the gap between the theory and the results became wider still. In the Brand treatment of typhoid fever, for instance, we were at first inclined to regard almost the whole of its beneficial effect as due to a mere mechanical lowering of the temperature and the escape of abnormal bodily heat. One after another our clinicians have come to the conclusion that this is one of the least of its beneficial effects, and that the singularly tonic effect which is produced upon the heart, nervous system and renal excretion is the central factor in its wonderful power.

All the leading authorities upon this method of treatment—Baruch, Osler, Seiler, Stockton—have expressed themselves most definitely to this effect. In the words of the last: "It is not simply a question of reducing the temperature, for it cannot be too strongly insisted that, while the temperature is an extremely important and constant accompaniment of these states and changes, it is far from being the most serious or the most important of them. In fact, it is to be regarded, both in its rise and reduction, as only an index of more important and active changes, which are going on deep in the interior of the body. So far as the mere reduction of temperature is concerned, the Brand method offers probably little advantage over the antipyretic drugs, but its remedial superiority lies chiefly in the effect it has upon the underlying factors. Authorities are agreed that the chief factor in its curative effect is not the mere mechanical reduction of temperature, as such, but the marked improvement in tone, first in the peripheral cutaneous and then in the general vascular system. This it is which drains and empties the engorged lymph spaces of their poisoned food materials, that relieves congestion in the hepatic and pulmonary circulations, that throws the full volume of blood through the anæmic, paralyzed kidneys."

Still more recently, in a widely divergent realm of therapeutics, this method has been applied, and even with more surprising results: first, in the treatment of the toxæmic heart-failure of pneumonia; and, secondly, in the so-called Schott method in the treatment of various heart-diseases. In the latter of these the effect upon the vascular mechanism is much the same as before—the application of cool or cold water to the body surface. This, however, is rendered more stimulating—first, by the addition of considerable quantities of salts, chiefly such as will be found in sea-water; and, secondly, in the later stages by the introduction of that unrivalled stimulant to unstriped muscle fibre, carbonic acid. In this last case we have obviously the temperature factor completely eliminated, and the nervous system as such almost equally so; for these patients are usually in a fairly good state of equilibrium, with but the one defect, the inadequacy of their great heart-pump.

So marked is the effect of this skin-heart tonic, that in severe cases of dilatation the almost incredible result is attained of causing the apex to retract three-quarters of an inch towards its normal position in a single bath. Not only are the pulsations of the heart greatly lowered in frequency, but apparently increased proportionally in power, so that the work which was previously altogether too much for it is performed with comparative ease and comfort.

In fact, the results obtained from this simple remedy, sound almost too good to be true, and would hardly be believed, if the repeated experience of clinicians did not almost unanimously verify them.

Now it seems to me that on no possible theory, which regards the heart as the sole motive force of the circulation, and the heart-muscle as the only muscle in the vascular system, possessing powers of rhythmic, propulsive contraction, can more than the merest fraction of any of these three great classes of results be explained. But if we recognize a power already suggested, of constant rhythmic contraction, upon the part of muscular tissue *wherever found* in the vascular system—grant this, and it seems to us that the problem in all three cases is well-nigh solved. The voluminousness and functional importance of the great mesh of bloodvessels in the skin and subcutaneous tissue, its importance as a heat-regulating and excretory factor, have been insisted upon by all physiologists; and if, in addition, we have the right to regard this enormous mesh, capable of containing nearly 30 per cent. of the entire blood of the body, as endowed with the power of independent contraction in its muscular walls, we have at once a factor in the circulation which could be depended upon for the production of some most striking results.

In fact, we venture to claim that in the bloodvessels of the skin and underlying tissues, we have in the higher vertebrates, just as everywhere in the tissues of the lower forms of life, a great "skin-heart," which plays an important part in the circulation, not only in health, but also in disease. For instance, in the effect of the Brand baths, the fact that the local stimulant effect upon the vessels of the skin is promptly followed by a rapid reactionary dilatation, is as familiar as the alphabet; but just why this reaction should so immensely improve the quality of the heart's action and relieve the toxic condition of the whole nervous system, is as yet hardly accurately explained. It is usually accounted for on the ground that it relieves the work of the heart by dilating the skin vessels and diminishing peripheral resistance.

But Winternitz observes, what a glance at the flushed skin of the fever patient would immediately suggest to the eye, that we have already a distended condition of the peripheral portion of the blood channels due to paralysis of the vessel walls, and insists in flat contradiction to the other explanation, that the heart's action is improved by the *restoration of resistance* in the peripheral circulation. But let us once admit the fundamental element in this so-called "improvement of the tone" in the superficial vessels, the appearance of which all investigators agree upon, is really an active and not a passive one, a local rather than a reflex change, and the problem is solved.

In other words, the normal condition of the muscles in the walls of the arterioles, and of the amœboid contractile endothelium of the capillaries is not one of rest, either in constriction or dilatation, but of constant rhythmic activity, and that the restoring of this active contractility in the vast mesh of vessels in the skin, by the contact of cold water and by friction, is the essential element in the improvement of the circulation. The heart itself is nothing but a special local aggregation of these same muscular fibres, and, like them, its action is intrinsic and merely *regulated* by the so-called cardiac nerves; and, when we again recall that the great contractile mesh of the cutaneous vessels is capable of containing over 30 per cent. of the entire blood of the body, and that the whole of this surface is affected by the cold bath, it hardly seems impossible that the stimulation of this great diffuse "skin-heart" may be a factor of the greatest importance in improving the entire circulation. Once this active addition to the total force of the circulation has been effected, the relieving of the lymph toxin-stagnation in all the tissues and organs follows rapidly. The nervous system, rid of the torturing poisons with which it has been saturated, most rapidly feels the relief. Sleep now becomes possible, and is simply the beginning of the benefits which will flow from this gain. The digestion is distinctly improved by the relief of the portal stagnation, and another important line of communication with the relief column is opened up. The marked improvement in the nerve, determination, and courage of the patient is but a striking symptom of the similar change which is taking place throughout the whole organization, and is of itself an immense gain in the struggle back to health. The kidneys are flushed by an abundance of blood, which both nourishes and stimulates them to increased excretory efforts. The glands of the skin, freed from the singular choking effects produced upon their spiral excretory ducts by the lymph stagnation in the surface tissues, resume their activity, and, according to Quirolo, the toxic properties of the sweat of fever patients are almost as well marked as those of their urine, and so the entire situation is modified in the right direction.

Now let us see of what assistance this hypothesis would be in explaining the remarkable effects of the Schott-Nauheim treatment. Upon what would these cool baths, with a high percentage of saline constituents in them, rendered still more stimulating by the addition of carbon dioxide, and prevented from depressing or chilling the system by passive movements and gentle friction, be most likely to act? Obviously upon the great skin-mesh. And when we remember that we are practically plunging the cells of this entire skin-heart into their old, ancestral medium of sea-water, and adding to it the one remedy which most powerfully increases peristaltic action on the part of any of the unstriped muscles of the body—as seen in animals poisoned by it—carbon dioxide, could we imagine anything which would be much more likely to stimulate to its highest degree of vigorous contraction, and restore to its molluscan and crustacean, long-swinging, tireless rhythm, the great skin-heart?

The effectiveness of carbon dioxide in stimulating and equalizing contraction of unstriped muscles, not only in the arterioles, but also in the walls of the bronchioles, has been most interestingly shown in Ewart's striking report upon the beneficial effects of inhalations of this gas in cardiac inadequacy and in asthma.

The first shock of the cold stimulates the whole mesh to contract forcibly and drive on the stagnant blood, not merely through the arterioles, but, by acting upon the contractile epithelium of the capillary walls, through the capillary system, by a similar stimulation of their linings and walls through the lymphatic and venous systems, the lymph which has become poison instead of food to the tissues. This, when thrown into the right side of the heart, provides the greatest stimulus for contraction of the ventricular muscle, namely, active dilatation by an abundance of blood. The lungs do their part in purifying, and return it to the left side of the heart, from which it is driven in abundant flow through the kidneys, thus accounting for the marked increase of urinary secretion after this treatment.

But if the action ended here, we should only be a little better off than before, for upon the principle usually accepted, the superficial blood vessels, having contracted, would remain for a considerable length of time in the same condition, and the heart would simply have to overcome on the arterial side precisely the same amount of force which had been added to it upon the venous. Suppose, however, that the contraction has been a rhythmic one, and that the vessels have dilated in readiness for this increased supply of purer blood, the moment they receive it, they again promptly contract and drive it on again into the greater veins. That this rhythmical contraction, as shown by a healthy flush of the skin, is steadily increased by the continued restoration of ancestral conditions, the vigorous sea-bath which the vessels are receiving is evident; and it seems to me that we really have in this new force added to the circulation, something like an adequate explanation of the method by which the weak and distended ventricle can succeed in retracting its apex half or three-quarters of an inch toward the median line, during a single sitting.

We would again insist upon the fact that neither in typhoid nor in cardiac inadequacy can these effects, or anything like them, be produced by cold alone (for that has been thoroughly tried in both cases), by the temporary application of water alone, of whatever temperature, or by either dry, saline, gaseous or mechanical irritants. It is absolutely necessary that not merely cold, but cold water, should be used; that the surface should be literally soaked in this for a considerable length of time; while the effect is markedly increased by the addition of the sea salt, and still further by carbonic acid, such as would result from abundant processes of oxidation in the water. In fact, fanciful, perhaps, as the suggestion may seem, it is by accurate imitation of our most ancient, ancestral surroundings, in cool sea-water of a high degree of salinity, and a considerable percentage of carbonic dioxide—in short, precisely the condition which we find in the shallow lagoons in which animal life probably originated—that we reach the maximum of curative effect.

I have been greatly pleased to learn, upon writing to our leading American authority upon hydrotherapy, Dr. Simon Baruch, that his experience has led him to an almost identical view; that, as he expressed it, the cold bath gives rise to an "active dilatation" of the skin vessels, "an active hyperæmia, by reason of which the blood is propelled more vigorously through them"; that "the Almighty himself could not have created an apparatus possessing sufficient force to propel a viscid fluid like blood through the fine vessels of the skin did not the latter possess propulsive powers," and that some such hypothesis as the "skin-heart" would be of great value in explaining some of the perplexing points in hydrotherapy.

Now, let us see for a moment what basis of probability exists for the presence of this factor in the present state of our physiological knowledge. Although, as I confessed at the beginning, little more than suggestions of its probability can be given, yet there are several of these. In the first place, all observers for the last thirty years have reported, from time to time, the appearance of rhythmic contractions in certain groups of the vessels of the lower forms, not merely in the invertebrates, but also in the lower vertebrates, and even in mammals. The further we go down the scale, the more frequent this becomes. In fact, in the invertebrates it may be regarded as the rule. Among the lower vertebrates the vessels in the wing of the bat, in the fin of the eel, in the fins of various fishes, and in the foot-web and mesentery of the frog have been repeatedly seen to possess the power of constant, though slow, rhythmic contraction. In many cases, this has been reported without any apparent suspicion of its real nature, as, for instance when the arterioles of the frog are reported to seem to "vary spontaneously"; and when, as Curtiss* states, in watching the capillary area in a rabbit's ear, "Capillaries not noted may suddenly spring to view," and shortly after disappear. Among mammals, almost every observer has commented, with varying resultant opinions, upon the singular rhythmic contraction frequently observed in the ear of the rabbit, and occasionally in the mesentery of the same animal. Curtiss also admits that the capillary walls are evidently "living cells, and possibly contractile." Porter declares that there has been much discussion over the rhythmic contractions present in some of the vascular areas of mammals; and these are but a few of dozens of admissions of the existence of such contractility, or occasional signs of it, in the mammalian bloodvessels.

Of course, it hardly needs to be said that it is only very occasionally that the opportunity for observing this process in the mammalian tissues can be obtained; and with the single exception of the ear of the rabbit, in which every observer has noticed it, the placing of the tissues in a position to permit of this change being noted, if it occurred, would necessitate, not only a very serious disturbance of the normal relations, but even of life itself. It is, to my mind, to say the least, suggestive that in the only places in the mammalian kingdom in which this phenomenon might readily be studied with the parts in the normal condition—the wing of the bat and the ear of the rabbit—it has been noted, and in some cases quite extensively speculated upon, by almost every observer. In fact, as Wesley Mills sums up the discussion of this phenomenon, "Such facts lend some colour to the view that the return of vessels to their previous size after distension by the cardiac systole is aided by the rhythmical

* "American Text-book of Physiology."

contractions of the muscle-cells in the walls."* But we must also admit that nearly every investigator who takes the trouble to definitely pronounce upon this question expresses himself practically in the words of Morrant Baker: "There appears to be no reason for supposing that the muscular coat assists to more than a very small degree in propelling the onward current of the blood."†

Finally, are there problems in the physiological aspects of the circulation which remain conspicuously unsolved, and in which this factor might play a part? There are three at at least. One of them is the much-disputed question of the *dicrotic* wave in the pulse, which has usually been explained as a reaction wave upon the part of the elastic coat of the vessels, as an oscillation reflected from the periphery, as a percussion wave from the closing of the aortic valve, and upon a variety of other grounds. Upon closer examination, this wave is usually found in reality to consist of a low plus pre-dicrotic and a higher dicrotic curve; and we cannot resist the suggestion that we have here precisely the condition which would be accounted for by supposing that the first recoil of the bloodvessel toward its normal calibre was carried out mechanically by the elastic tissue in its walls, producing the pre-dicrotic oscillation, while its return was completed by the active contraction of the muscular coat producing the dicrotic wave proper. Moreover, this condition of affairs is exaggerated and retarded by lowered arterial tone; by which is meant a relaxed condition of the muscular coat, and consequently a free and complete distension, followed by a slow contraction of wider range, corresponding to the degree of distension. In conditions which increase the arterial tone, in which the distension from yielding is slight, and the

* "Animal Physiology.

† "Kirkes' Physiology," p. 207.

reaction so prompt as to practically coincide with the recoil of the elastic tissue, not only are the two waves merged into one, but their beginning is so nearly synchronous with its cessation of distension that the downward curve is practically uninterrupted, and the dicrotic wave almost disappears in high arterial tension.

I have been assured by my colleague, Dr. Hopkins, that he became convinced some years ago, as the result of an extensive study of syphmographic tracings in the wards of the Buffalo General Hospital, that some active participation in the propulsion of the blood, upon the part of the arterial wall, was absolutely necessary to explain in any adequate way, the phenomena of the dicrotic wave; whilst all physiologists agree with Porter, that, "although the origin of the dicrotic oscillation has been much discussed, it is not yet satisfactorily settled, important as the bearings of such a decision would be."*

And, last of all, there are certain reactions in the wonderfully complex and interesting problem of the maintenance of the blood pressure, which still lack anything like satisfactory explanation, on the usually accepted hypothesis of the passive relation of the arterial walls. For instance, the familiar increase of general arterial pressure where an increased amount of blood is being driven through a part, is precisely the opposite of what would be expected on *a priori* grounds, from the action of the vessels, were they mere passive conducting tubes. This has usually been lamely explained by calling into play that mythical power of the long-suffering heart, of increasing the work done by it in direct proportion to the resistance offered to it: which, if true (except for a limited period), would place it upon a perfectly abnormal pinnacle of biological virtue. Supposing however, that this

* "American Text-Book of Physiology."

increase of the arterial pressure is due to the active propulsive pressure which the muscle wall is exerting upon the blood, and that its contractions occur at the same rate with those of the heart, but in the intervals between them; then we can at once see how the blood-pressure may be distinctly raised, and yet the work of the heart not only be not increased, but even diminished thereby.

In fine, we would venture to submit these conclusions, as a basis for further investigation and discussion :—

First, that the existence of active contractility upon the part of the muscular wall of the arteries and arterioles, and in less degree of the veins and lymphatics, and of the capillary epithelium, is something which we have the strongest reason to expect, upon ancestral grounds, in even the highest mammals.

Secondly, that the beneficial effects of cold water upon the circulation, particularly of water of a high degree of salinity and accompanied by friction, first in health, secondly in the Brand method, and thirdly in the Schott-Nauheim method in cardiac disease, are only adequately to be explained upon the ground of the persistence of such a power in our mammalian skin-heart.

Thirdly, that the occurrence of this sort of contraction is almost uniform in invertebrates, and has been observed in the vascular area of many of the lower vertebrates—frogs and fishes, and in those positions in which it could be readily seen under normal conditions in the higher vertebrates—namely, the wing of the bat and the ear of the rabbit. So that we have abundant grounds for the possibility, and some even for the probability, of its occurrence in our own species.

Fourthly, that in the behaviour of the vessels in health, as noted by physiologic investigators, there are again conditions which are confessedly unexplained, and yet which may be accounted for on this supposition—the rhythmic pulsation of the vessels in the rabbit's ear, the restoration of normal tone on the part of the vessels of any area, after recovery from section of the vaso-motor nerves, the persistence of contraction in the ventricle in lower vertebrates and in the auricle in all forms, after section of all the cardiac nerves, the phenomenon of the dicrotic wave, and the anomaly of an increase in the rapidity of the circulation and amount of blood in a given part, coinciding with marked increase of the arterial resistance.

Can we discover any phenomena of reversion or ancestral tendencies of any sort, in the diseases of the second great vascular tissue, the fluid core of the blood vessels, the blood? This, like any other tissue of the body, is composed of cells, which are bathed in a fluid medium, only, instead of the cells being bound closely together, and the fluid medium small in amount, as in the fixed tissues, the fluid medium is abundant and the cells are in no way connected with each other. It cannot, however, be too strongly insisted upon that, in spite of the disrepute into which the terms "blood disease" and "blood out of order" have fallen, it is a distinct and uniform tissue, and subject to disturbances of nutrition, which are just as definite and peculiar to itself as those of the liver or the kidney. To leave out of account those singular disturbances of its chemical composition to which it appears liable, chiefly as the great circulating medium and nutrition carrier between all the fixed cells of the body, it has distinct structural disorders, to which as a class we give the name of anæmias. Like other structural disorders, these are chiefly signalized, or rather, in the present imperfect state of our knowledge, can only be definitely detected by changes which take place in the cellular composition of the tissue.

The blood is a tissue of almost as uniform bulk as any other in the body, for, except in certain extreme conditions, its actual volume changes very little indeed; and its methods of departure from the normal are of the two great kinds, the primary or cellular, and the secondary or plasmo-chemical. It has hitherto been customary in our study of the varying conditions in the cellular structure of the blood to confine our attention almost exclusively to the presence, the number and condition of the so-called higher class of its cells, the red corpuscles or erythrocytes. For purposes of classification this method may perhaps still be adhered to, especially as this is the element in the blood which can be most readily estimated, and in the present state of our knowledge we are still unprepared to say anything very definite as to the disturbances of the white cells. However, as has already been seen in the study of the individuality of the cells, it is probable that the latter play an equally important, and under some conditions, an even more important function than the higher, and that the time will come when we shall have a classification of disturbances of the blood, based upon our study of the number and conditions of the white cells. Already we are beginning to regard the leucocyte-count as one of the most important indications of the resisting-power of the system, in several of the infections, notably in pneumonia, typhoid and tuberculosis; and, as will be seen in our discussion of the red variations of the blood, a substitution action on the part of the white cells is a most important factor in the development of their course. In fact, in the later stages and severer forms of the anæmias, this leukæmia is regarded as one of the chief morbid symptoms.

The pedigree of the blood has already been alluded to both in the fœtus and in the family tree, first consisting, apparently of a non-corpuscular watery fluid; then, in the higher Metazoa and in the Molluscs and Crustaceans, beginning to possess corpuscular elements of an amœboid character. Still higher in the last of these classes, colouring materials begin to appear, although at first these are not contained in the corpuscles, but are dissolved or float in crystalline form in the serum. The prevailing colour of the blood in the molluscan and crustacean stage is of a bluish or greenish tint, which appearance, according to the investigations of Haycraft, is chiefly due to the presence of copper salts, which, together with manganese, appear to play much the same part in the higher invertebrate blood, that iron and its salts do in the vertebrate. So that the term "blue blood," as indicative of extreme antiquity of descent, is found to have a most unexpected biologic endorsement.

In a few of the highest invertebrates we find the appearance of a new class of blood-cells which, absorbing the colouring matter from the plasma, begin to form a class of their own—the so-called coloured corpuscles. In the earlier stages, this colouring matter which they absorb is a greenish pigment, in some cases quite closely allied to chlorophyll, and in others consisting of salts of copper. And it is, to say the least of it, a curious coincidence that the so-called "red" cells of mammalian blood are, when studied singly, and by transmitted light, of a distinctly greenish colour; and that in certain tumors of embryonic tissue type (chloroma and myxo-sarcoma) we also find a distinct greenish tint, like the fat of a turtle.

These cells in the lowest vertebrates, notably in the frog and the salamander, are still quite different from the red cell of the mammal. In the first place, they possess a distinct nucleus, they are of great size, and they are almost uniformly oval in shape; and this condition of affairs remains practically the same through the reptile class, until we reach the essentially warm-blooded vertebrates, the birds and the mammals. Here the red cells experience a very decided change, they have lost their nuclei, have assumed a circular, disc-like form, and have diminished to about one quarter of their amphibian size; and this fineness of division appears to correspond roughly with the degree of activity and the normal temperature of the organism. In fact, from the Cœlenterate Lumbricus, with its white-blood cell of 1-120th of an inch in diameter and no red cells, and a temperature only six or seven degrees above that of the surrounding air, up to the swallow with a red cell about 1-6000th of an inch in diameter, and a temperature of 108° to 110° F., there would appear to be an almost uninterrupted series of changes, of diminution in size, and increase in brilliancy of colour of the blood cells, with a rising temperature and a correspondingly high degree of vital activity.

In the fœtus we find almost precisely the same series of changes taking place, with the exception of the bluish or greenish tint of the coloured cell, and that observers are somewhat divided as to whether the nucleated red or white cell is the first one to be budded off from the inner wall of the bloodvessel. Certain it is, however, that we have an amœboid white cell appearing at a very early time, and simultaneously a nucleated red cell, which persists all through fœtal life, spheroidal with a granular nucleus (Ichthyopsidian), and totally disappears at birth or within a few months of it, except in some of the innermost recesses of the body—the red-bone marrow—to reappear, as we shall see, in certain conditions of disease. In other words, as long as the human fœtus is a submarine organism, living at the amphibian stage, its blood closely corresponds to that of its ancestors of the same grade of development. When, however, we come to consider the interesting and most important question, what is the actual ancestry of the so-called higher form, the red-blood plastid, we find ourselves at once in the midst of a hotly-contested battle of theories. For a considerable time, the universally accepted position was that the red plastid was a white cell, which had undergone development in a special direction, and a desperate attempt was made to prove the presence of a nucleus and the existence of a cell wall. But both these latter positions had to be ultimately completely abandoned, for the behaviour of the red cell in various reagents, and its loose grip upon its hæmoglobin, have finally proved that it posseses neither the one nor the other ; although, under certain conditions, it appears to possess the power of slight amœboid movements.

The next suggestion was that its ancestry was direct from the nucleated red cells, which, as is well known, are budded from the inner wall of vessels in the growing vascular areas of the embryo: and a very beautiful and attractive theory was built up, of which Howell was the principal champion, according to which, by a process of extrusion of the nucleus, the embryonic or ancestral nucleated red cell became transformed into the adult erythrocyte. This was chiefly based upon the series of observations by Howell, in which he had actually seen this extrusion occur. Later and more careful investigations, however—notably those of Minot and Schäfer —cast decided discredit upon this view by showing, first, that the nucleated red cell totally and apparently finally disappeared from, so far as could be found, every tissue of the infant within a few months after birth, while the red cell, of course, is produced in abundance all through this period. Secondly, that the nucleated red cell is found only in very small numbers indeed, in those areas—the red-bone marrow and the spleen—in which the birth of the red corpuscle is most rapidly occurring; and, finally, by repeating and extending the observations upon the extrusion of the nucleus, they discovered that the body of the nucleated red cell, after losing its nucleus, simply went to pieces, and that extrusion was merely a step in the process of its death and absorption. So that we are again brought back or—more correctly—shut up, to some form of the old original hypothesis: that, whereas we can demonstrate the abundant production of the white cell in the lymph areas, serous cavities, and adenoid tissue generally, of the body, and can nowhere distinctly trace the birth of the red from any of the fixed tisues, although some important step in their development is unquestionably carried out in the red marrow of bones, the high probability appears to be that the red corpuscle is in some way and by some step, as yet uncertain, descended from the white.

One important modification, however, has been practically finally settled, and that is that the red corpuscle of the blood is in no true sense a *cell* at all, but probably a mass of chromatin-granules, threads and nuclear stuff, analogous in its nature to the chlorophyll granule of the plant-cell. So strongly is this insisted upon by the more recent investigators, that both Minot and Cabot decline to apply the term "cell" and "cyte" in any form to the red corpuscle, and demand that they should be known as "plastids," or some other term expressing that they are a mere product of cell activity and not independent individual cells.

Now, let us see what bearing the individual descent and ancestral history of our blood-tissue has upon its changes in disease. Hitherto, as we have said, we have largely limited our study of the blood, and classified its disturbances according to the number and condition of the red cells; and upon this ground we may roughly divide all its commonest disturbances into three main classes; the, so to speak, functional disturbances of the red plastids, in which merely their proportion of hæmoglobin is deficient, the chloroses; second, the simple anæmias proper, in which there is not merely deficiency of the hæmoglobin, but diminution in the number of the red plastids, without, as yet, any very marked "substitution" increase upon the part of the whites; and, finally, we have the group in which this "substitution" process has reached such a tremendous activity as to have become the most striking factor in the situation—the leukæmias and leucocythæmias.

This, of course, is only a rough division upon biologic grounds, and is merely adopted for purposes of convenience in discussion, with a clear recognition of the fact that each one of these classes may be, and often is, simply a stage in the progressive development of blood deterioration in one and the same case. In disturbances of the first class we probably have to do chiefly with the simple destruction of the red plastids at a more rapid rate than the normal processes of their production will keep pace with; which destruction appears to be most frequently due, either to the extraordinary drain upon the body tissues at the time of puberty, or to the "choking" of the hæmoglobin, in the portal circulation, by gases or toxins absorbed from the alimentary canal. Indeed, it seems highly probable that this is the incipient stage of nearly all the severer forms of the disease, even of the so-called "essential," or "pernicious" modification. Here, we have an illustration of a carefully developed chemical affinity, on the part of a certain class of cells, which is of vital importance to the body, leading under slightly changed conditions to their own destruction. The blood plastid owes its presence in and usefulness to the entire organism, and its powerful affinity for oxgyen, or carbon dioxide to its contained hæmoglobin. Unfortunately, however, this same affinity is equally great for the various sulphur, or cyanogen gases, and their compounds; and the epithelium of the alimentary canal, reverting to its old, ancestral, respiratory function and breathing these into the blood, the mere chemotactic power of the plastid, which has been so carefully refined upon and specialized, is the means of its instant destruction, whenever it is brought within reach of these poisons.

This having occurred, they can no longer perform their proper oxidation processes in other parts of the body; the tissues being lowered in their nutrition, tend to undergo a certain amount of fatty degeneration, such as is artificially produced in geese and fowls by repeated bleedings during the fattening process, and we have the characteristic plumpness. The respiration, of course, suffers chiefly; but unless the disease goes to the stage where the red plastids are actually destroyed, instead of being simply robbed of their hæmoglobin, the recuperative powers of the system are usually sufficient to result in recovery. Later, however, either the poisoning is more violent or prolonged, or the recuperative powers of the system, for some reason, markedly depressed, and it is only a step from this purely functional form to the much more serious "grave anæmia," as it is termed, and often ultimately apparently to the pernicious form itself.

In such case, the disease passes into our second class, where there begins to be a marked deficiency, not merely of hæmoglobin, but of the red plastids themselves; and, according to the resisting power of the system, it may follow either of two lines of development, the one in fairly vigorous subjects, where there is an abundant production of the white cells, apparently in order to endeavour to supply the deficiency of the red products, and we get the so-called "leukæmia." In the other, although this reaction occurs to some degree, yet it is so slight as to practically produce but little effect, either upon the blood-count or the course of the disease, and the chief factor in the situation is an enormous and progressive diminution of the red plastids; and, if no primary substitution process upon the part of nature occurs, or if the second step—the development of the white into the red—be prevented from occurring, this may ultimately result in the fatal "pernicious" form. At the same time, distorted forms of the red cells appear, both megalocytes and microcytes, and, even more constant and diagnostically characteristic, we have a sudden reappearance upon the stage of the nucleated red cell, which also actually possesses an oval shape, while the tissues become of a singular greenish or lemon-yellow sort of tint, as even the popular name for the earlier stages of the disease, the "green sickness," expresses.

Now, what have we here from an ancestral standpoint? Simply the disappearance, more or less complete, of those elements (the red plastids) which, as we have seen, are characteristic of life at the mammalian level; a reappearance of the old, oval, nucleated red cell, and abundant white cells of amphibian life; and, what I should hardly care to mention, except as a curious coincidence, the occurrence of some change in the blood which gives the old crustacean colouring to the tissues. In short, we have a reversion upon the part of our blood to the amphibian stage, and all the activities of the body follow suit; the temperature is maintained with great difficulty, the heart's action becomes feeble and dicrotic, the movements of the body have to be of the slowest and most infrequent character, in fact, not only the blood, but all life sinks at once to the turtle stage. I find that this reappearance of the oval, nucleated red cell has already been commented upon, as a probable reversion, by Wesley Mills among the physiologists, and by Henry among the clinicians.

Supposing, now, that another of our imaginary cases has possessed sufficient recuperative power, upon the part of its lymphoid (embryonic) tissues, to make an attempt at breeding up enough leucocytes to fill the gaps in the "thin red line." Again there are two courses open. If the comparatively simple and easy excessive breeding, upon the part of the lymphoid tissues, is not handicapped by some grave inability, either on the part of its products, the lymphocytes, to change into the red plastids, or of the erythrocyte breeding cells of the bone-marrow to perform their function, then the deficiency will be made good, and recovery will occur. If, on the other hand, the lymph glands indeed do their part, but, from some toxic condition of the fluids, the red bone-marrow can no longer do either its transforming or original production-work, or can do it but badly, we have only a partial substitution for lost cells, so that the blood-count sinks to perhaps two million, and is maintained there fairly steadily, while a piling-up of the primitive product results and we have that enormous increase not merely in the number of cells, but even in the actual volume of the blood apparently, which we term "leukæmia." Here it is worth noting that by far the greater part of the increase is in the simplest and most primitive form of cells—the lymphocytes. Again the cells of the red marrow try to restore the balance by dropping back to their old ancestral power of producing nucleated red cells; again these or the polynuclear leucocytes reproduce prematurely in an abortive attempt to make good the red deficiency, and we have the poikilocytic condition, with its distorted and occasionally nucleated small red cells; again we have the singular tendency to the appearance of the green colouration: the clot in the heart after death has been described by several observers as of such a vivid green colour as to recall the fat of the turtle, well known to all epicures. Not only that, but, as Dock has shown, the singular "green cancer," or chloroma, with its striking colour, is a lymphoma closely allied to the overgrowth of the extreme stage (as we believe) of this process—Hodgkin's disease. I have myself seen this green colouring in two cases of myxo-sarcoma removed in Dr. Roswell Park's clinic. Again, the body temperature falls, the heart's action becomes feeble and dicrotic, muscular movements are reduced to the barest possibility of contraction, competent to maintain life —in fact, the blood has sunk even more emphatically than before to the crustacean stage, and activity has fallen to the molluscan level.

Last of all, in the development of the drama, we come to those extraordinary cases in which, if we might still consider them lineal descendants of our four primary cases, the destruction of the reds has occurred, the increase of the whites has followed to a certain degree; but this increase has been so difficult upon the part of the lymph-nodes and the spleen, that they have been, as it were, unable to completely set free their product, and, instead of producing free cells which have gone to enrich the blood, they have developed an enormous increase in their embryonic fixed substance, and we get the huge lymph-node enlargements of Hodgkin's disease, or pseudo-leukæmia. The message, so to speak, seems to have reached the cells; they have responded to it as far as the reproductive process is concerned, but they have been unable to carry their product far enough to make it of any benefit to the system, and it has simply been piled up upon itself.

To sum up, while distinctly disclaiming any attempt to show that these various stages are actually lineally descended one from another in the same patient, or that the later forms necessarily pass through the earlier in the course of their development, and admitting that the descent of the red cell from the white is not clearly proven, it does seem as though, from a morphologic standpoint, there had been a great series of successive steps in the deterioration of the blood tissue and its component cells. First, a failure upon the part of the red plastids to maintain their quota of hæmoglobin; second, an inability of the white cells or bone-marrow cells to produce their ultimate product; and, third, a "rebellion" on the part of the birth-areas of these same cells, the lymph-nodes, in which they multiply excessively, without subserving the welfare of the body. And that, in any case of disease, we find that the blood-tissue is unmade in strikingly similar "reverse" order to that in which it was made.

Our knowledge of the slighter disturbances in the blood of animals is most limited for obvious reasons. The absence of striking or characteristic symptoms in the earlier stage, the complete pigmentation or covering by hair of the skin, thus preventing the recognition of their most striking single symptom, changes in colour of the transparent human skin, the infrequency of the blood-count for diagnostic purposes in veterinary practice, make chloroses and simple anæmias in animals most difficult of recognition. *Symptomatic anæmias* of considerable severity are, however, not uncommon, and are chiefly due to three great groups of causes, excessive lactation, wasting disease, and the attacks of parasites. The first class are comparatively frequent in cows, goats, ewes, and bitches, especially if their food-supply be of poor quality. The group due to wasting diseases occur just as in our own species, and appear fairly common in wild animals in captivity, especially during tuberculosis in monkeys and in graminivorous birds.

The last class is, however, by far the most common; any of the innumerable filariæ, strongyles, trichocephali (anchylostoma), trematodes of mammals, and cytodites of birds which swarm in the blood, lungs, intestine, stomach and liver may, under conditions of depression, produce profound anæmia. The changes in the blood may be even more marked than in our own species, 2,000,000 red plastids per cubic m.m. instead of the normal mammalian average of 7,500,000. Nucleated red cells are also found, and numbers of small and distorted erythrocytes.

Cases of idiopathic *pernicious anæmia* have also been reported in the horse and the mule, in fact, epidemics of the disease have been described in Europe, India and Siberia. But these latter, upon closer investigation, have been found due to the presence of organisms in the blood, the European form to minute bacilli (Zschokke, Friedberger), and the Asiatic (Surra) to a motile spirillum which destroys the red plastids (Evans, Burke, Ignatovsky).

I have found one well-marked case of pernicious anæmia in an orang-outang which had lived for some years in the ape-house at Regent's Park. All the viscera and tissues were pale and œdematous, the liver and kidneys were white and fatty, the pericardium full of milky fluid, the veins apparently almost empty of blood, which was of a light pinkish colour, more like tinted milk than blood.

The conjunctivæ and other mucous membranes had been blanched for months before the animal's death, and the symptoms had been those of a steady decline of heart-power, and increasing shortness of breath on exertion.

Leucocythæmia, with all the characteristic changes in the corpuscles, lymph-nodes, and bone-marrow, has been seen chiefly in dogs, but also in the horse, ox, pig, cat and mouse. Nocard has collected 22 cases in the dog, 9 in the horse, 6 in cattle, 5 in the pig, and 1 in the cat. The blood becomes a pale rose colour or greyish brown, and the ratio of the white corpuscles to the red has been found as high as 1 : 45, 1 : 20, 1 : 12 (Forestier and Siedamgrotsky), (Law). The normal average in the domesticated animals being 1 : 900, according to Nocard.

Lymphadenoma, or Hodgkin's disease, has also been found in the horse, the dog, and the pig. The cervical glands are first affected, so that in the early stage it may be mistaken for glanders; then those of the thorax and mesentery; and finally the adenoid tissue of the spleen, the agminate glands of the intestine, and the tonsils. Nocard has found masses of lumbar glands in the horse weighing 16 lbs., 20 lbs., and even 29 lbs. Leisering found the spleen in a horse, 3 ft. long, and weighing 28 lbs.; Bollinger, a pig's spleen of 3½ lbs; and Siedamgrotsky, a dog's exceeding 2 lbs. (Law). Peyer's patches may form rounded masses of lymphoid tissue an inch in thickness.

A most curious and unique alteration in the blood takes place in the horse, known as *acute hæmoglobinæmia*, or popularly as "black strangury." As its names imply, it is characterized by the sudden appearance of broken-down hæmoglobin or hæmatin in the blood and in the urine in large quantities. As, however, the changes which produce this are now known not to take place in the blood, but in the cells of the voluntary muscles, especially those of the lumbar region and hind-quarters, it is obviously not to be classed as a hæmic disease. Its onset is marked by sudden stiffness and soreness, rapidly developing into complete loss of power in the muscles of the back and hind-quarters, so violent and swift in its course as to have been at one time regarded as a form of paralysis.

The disease is well known and greatly dreaded by horse-owners, as it is not only very fatal, often barely 30 per cent. recovering, but seems specially prone to attack vigorous horses in the prime of life. In spite of most careful examinations of the affected muscles, no causal organism has yet been discovered, and we are completely in the dark as to the etiology of this strange degenerative myositis. The only predisposing condition known is over-feeding and idleness after heavy work, as it is most apt to attack city work horses in high condition, and stallions just after the breeding season. Indeed, in many of our large American cartage and express stables it is known among the ostlers as the "Monday-morning disease," as it is most apt to appear on that day of the week, after thirty-six hours' rest and high feeding. It does not appear to be infectious, although it will often attack three or four horses in the same stable within a few days.

CHAPTER VIII.

Diseases of the Skin and Kidneys.

To link together in the same chapter two such widely separated groups of diseases, as dermal and renal, may appear at first sight a decidedly arbitrary, if not indiscriminate proceeding. But from the comparative point of view they have not only a common basis, but many points of similarity. The difference between the coiled tubes of the sweat-glands and the *tubuli contorti* of the renal cortex, is that the latter have clustered themselves together in myriads and withdrawn into one situation deep in the interior of the body, while the former remain thinly scattered all over its surface. Their origin and function are identical, their products extremely similar, and they still manifest a marked sympathy with each other's condition, both in health and disease. Nor is this the only important organ or system united closely to the great skin-sheet by ties of blood. The most striking thing about it, from an ancestral standpoint is the number and importance of its blood-relatives.

The skin has suffered many things—in more senses than one—and been seriously misunderstood clinically, simply from the fact that it is the most external and superficial of our organs. It lies on the surface, and consequently has come to be regarded as a mere limiting membrane of the body, a waterproof, mechanical coating, its maladies only "skin-deep," requiring nothing but local remedies. No wonder that the treatment of its diseases was for centuries one of the chief opprobria of medicine, and that these latter came to be divided into the three celebrated classes of "those that sulphur could cure, those that mercury would cure, and those that nothing would cure."

But when we remember that one little strip of the ectoderm upon the ventral surface of the embryo, folding in and rolling up upon itself, forms the veritable core of the entire body, the alimentary canal, the food-tube and all its appendages; that another shallow gutter of the same on the dorsal aspect, dipping into the mesoblast, solidifies into the cord and balloons into the brain; that three little pairs of pits cephalad, burrowing between the gill-pouches, draw in enough of it to form the olfactory plates, retinæ, and organs of Corti; in short, when we realize that this wonderful skin-sheet and its descendants were the creators and remain the hereditary kings of this entire body of ours, then, and then only, do we begin to appreciate the extraordinary complexity of its relations, and the frequent and active sympathies which it manifests in both health and disease, with disturbances of almost every important system in the organism.

And the present functions of what was left of it, after making the food-tube and the nervous system, are by no means insignificant. It is the great heat-regulating organ (the more closely we study fever, the more we become convinced that it is chiefly due to disturbances of the thermolytic mechanisms of the skin), it is also an excretory organ second only to its descendants, the kidneys. Its blood-mesh is an important factor in the circulation, while it would require the united powers of the artist, the poet, and the physiologist, to do justice to its superb and matchless protective powers. A tissue which is silk to the touch, the most exquisitely beautiful surface in the universe to the eye, and yet a wall of adamant against hostile attack.

Impervious alike, by virtue of its wonderful, responsive vitality to moisture and drought, cold and heat, electrical changes, hostile bacteria, the most virulent of poisons, and the deadliest of gases, it is one of the real Wonders of the World. No product of the loom or factory can match it at even a *single* point, let alone possessing all of them. More beautiful than velvet, softer and more pliable than silk, more impervious than rubber, more durable under exposure than steel, well-nigh as resistant to electric currents as glass, it is one of the toughest and most danger-proof substances in the three kingdoms of nature. And yet, simply because it is naked and white and soft, we speak of it as "defenceless," like a clam that has lost its shell, and hardly dare permit it to see the sunlight or breathe the open air. Hence two-thirds of its diseases.

I may, perhaps, be pardoned for insisting at some length upon what may be termed the dignity and importance of the skin, as an organ, for I believe that a fuller recognition of this fact is the most important contribution which evolutionary pathology has to make to a knowledge of its diseases. Its hereditary relations and ancestral tendencies will be found to crop out at every turn in the realm of dermatology; all the school of "localists" to the contrary notwithstanding.

The length and fascinating interest of its pedigree alone would be sufficient to throw grave doubt upon the modern "superficial" view of its disorders. One of the earliest "organs" possessed by unicellular organisms, both vegetable and animal, is a cell-membrane, and this rapidly develops into the characteristic epiderm of plants with its permanent layers of cells. Growth proceeds from the inner layer, and the outer ones dry up, flatten, and scale off precisely as upon our own surfaces. The outer scaly layer, whether of bark or leaf, protects the inner juicy ones from injury; and let this be injured by mechanical abrasion, attack of parasites, or heat, or frost, and a reparative secretion is promptly poured out. Many of these exudates are highly viscous, so as to entangle attacking insects, like the "gums" of the fruit-trees, the acacias, and the rubber plants; others are extremely bitter, and often powerful insecticides, like the "milk" of the euphorbiaceæ, the lettuces and sow-thistles. Nearly all form on drying a tough paste, or parchment-like membrane, a perfect "aseptic dressing" for the wounded surface, while the well-known resins of the conifers, combine all four of these properties.

It may be only a coincidence, but I cannot help thinking that this wonderful exudate has something to do with the fact that the cone-bearers, with their mere handful of species, are the hardiest, the thriftiest, the most widely distributed of all our Northern trees. Certainly, it is the very essence of the renowned value of their timber for structural purposes, and the richer this is in resin, the greater is its resistance not alone to weather, but to the fungi of "dry rot" and to insects. And their only rival either upon the rocky and tempest-swept mountain summit, or along the dead-line of the Arctic Caribou-Barrens is the white birch, whose blanket-like bark is as impervious to both parasites and frost as an asbestos packing.

In other plants, this secretion becomes even more ingeniously protective, not merely becoming poisonous, but collecting itself in little cup-like recesses at the base of hollow hairs, to be discharged rattle-snake fashion into the tissues of the first assailant, as in the stinging-nettle. By such indirect and purposeful-looking methods as becoming saccharine, so as to attract ants, who will clear it of parasitic insects, or bees and butterflies to fertilize it. But we shall not pursue the subject further, as we hope to discuss it in full in a later chapter; our only purpose now is to bring forward a working base for the contention that in this markedly beneficent exudate from the vegetable epiderm we have the original ancestor of eczema with its "weepings" and crusts, and that the high bactericidal powers of the nasal mucus date from a very remote antiquity.

In short, the plant-epiderm reaches a plane of development but little inferior to that of the animal in either its bulk or appendages, except in one respect, that it has no power of invaginating itself, of pouching or burrowing for further specialisations. It forms its leaf-lungs above and its root-stomach below, but it never can divert its metabolic surface-sheet towards its interior. The animal has added this single power, and this alone; is a plant "turned outside-in," in fact. And we believe that this power of invagination will be found to be one of the most constant and distinguishing landmarks between the two kingdoms, in fact the very key-note of all animal superiority. This it is that enables animals to keep alive at their core and harden their surfaces, instead of having to rot the sooner at the heart, the faster they grow at the periphery.

We still have one tissue in the body which grows "tree-fashion," and dies at the centre with equal certainty and promptness, the crystalline lens. Cataract is the legitimate result of a plant-issue in an animal body.

The vicissitudes of the skin in its progress through the animal kingdom, though infinitely varied and interesting, are so familiar that the merest *résumé* is sufficient to recall them. The thick lime-layer which it lays down upon the surface of the Mollusca, the thinner and tougher lime-horn compound of the Crustacea, the tough keratin and chitin of the Insecta, the supple, india-rubber-like, "fireproof" coat of the salamander and frog, the armoured plates and scales of fishes, many of them with true bone in their interior, just like that later descendant the mammalian tooth, the rippling chain-armour of snakes, the plumes of birds, the fur of mammals—are but samples of its boundless resources and inexhaustible fertility in expedients. Like Voltaire's "Habakkuk," the skin is literally "*capable de tout.*" And any portion of the great primitive surface sheet (ecto- or endo-blast) in *any* organ of *any* species, has the whole range of these possibilities within itself, and will at times display them in the most unexpected manner.

The highly complex power of tooth-formation, which in mammals has become the exclusive monopoly of the alveolar epithelium, is possessed by the entire living epithelium of the mouth-parts, palate, fauces, tongue, and gullet in fishes, in crustacea and worms by the stomach itself (gastric mill), while in certain reptiles (Heloderma) there are "bosses" upon the snout and face which, though to the naked eye seem horn-like scales, upon section are histologically teeth; in fact, we now have an unbroken series between the simple fish scale through the bone-lined sturgeon scale (placoid) to the dentine-enamel tooth. Is it any wonder that dermoid cysts from any part of the body may contain teeth?

The horny transformation is an equally universal faculty, from the common and necessary "toughening" of the palms and soles of every group, by insensible gradations, by one route, through the "wart" or "corn," into the nail, the claw, the horn (of which last transition any part of the human skin may furnish an instance); by another, through the scale into the hair on one side, and the feather on the other.

The hair and the feather both appear as fine striations of the keratin at the base of the scales of certain armadillo-like reptiles on the one hand, and bird-like ones on the other, and are still formed under a horny sheet (epitrichium) in all bird and mammalian embryos, including our own. So that the production of hairs by the scaly epithelium of the conjunctiva and buccal pouches in mammals, including (pathologically) man, and by the cylindrical epithelium of the stomach in birds, as in the singular hairy pyloric ring in the canal of the grebe (*Plotus anhinga*), to say nothing of their almost constant appearance in dermoid cysts, are simply assertions of ancestral faculties and rights.

In short, nine-tenths of the diseases of the skin which result in the production of some new morphologic development, such as clavus, cornu cutaneum, verruca, hypertrichosis, ichthyosis, and also acne, eczema, and possibly pemphigus, are either reversions to ancestral conditions or the results of attempts in that direction. Not only this, but (what was the principal purpose of this hasty review of its protean possibilities) every one of these varied transformations has been effected and rendered possible by one single, simple process, that of burrowing or pouching, the only difference between the scale and the gland being the *direction* of the pouch or fold, outward (peripherally) in the scale, inward (centrally) in the gland, and between the gland and the hair or tooth that the pouch *turns back upon* itself (like a glove-finger starting to turn inside out) in the latter, and goes on branching into the interior in the former.

The principal "*Leit motif*" in the deadly drama of cancer, played only by the great skin sheet and its descendants, is this very power of burrowing and "nest" forming. As will be shown in a later chapter, the cancer "nest" is simply a gland pouch gone wrong, and the rate of progress of carcinoma is in exact proportion to the degree of this "pouching" power possessed by the epithelium in which it starts, varying from the slow, almost benign, "flat-celled" cancer, "rodent ulcer" of the pavement cells of the skin, to the hopeless and rapidly fatal cylindroma, "encephaloid" of the columnar and honeycomb-like epithelium of the pylorus, pancreas, or liver. The possibility of glands, hair, and teeth *includes* necessarily the possibility of cancer.

Is it possible to trace ancestral tendencies in any of our more acute skin diseases? We believe so, in two at least, and these the most frequent of all, eczema and acne. The former of these is so absolutely ubiquitous that this alone gives it the appearance, at least, of a natural process. Its scarlet banner floats over from 60 to 70 per cent. of all *recorded* cases of skin disease, according to Bulkley and Duhring; and when we recall the large amount of it which is simply dubbed "prickly heat," "scald," or "chafe," and cured by home remedies without calling any physician's attention to it at all, its actual prevalence must be rated even wider. Its spread through the range of living matter is equally universal, the "scab" of apples and potatoes, many of the "manges" of dogs and horses, the "grease" and saddle-galls of the latter, the "scabs" of the pig, the ox, the goat, are all eczemas, most of them of mycotic origin.

And yet, innumerable as are the forms assumed by it and appalling the list of pompous terms invented to distinguish them (nearly sixty of which disfigure our text-books, and torture the student mind with an ingenuity worthy of the Inquisition), a single process of the utmost simplicity is at the bottom of them,—"weeping," or the formation of drops of semi-fluid exudate all over the affected surface. Let these drops be small and slow of formation, so as not to tear loose the horny layer, and we have the "papular" form, larger or more rapid, and they lift up the latter and form a tiny pool between it and the mucosa, and we say "vesicular." Is the irritation a shade more violent, corpuscles are poured out as well as serum, and by dying turn the pools into pus, and the pustular eruption is before us; rupture the vesicles or pustules by scratching, and their contents dry down into scales or crusts, and so on through the whole gamut.

I cannot help believing that we have here a true homologue, if not an actual reproduction of the old ancestral "bleeding," oozing, or gum-forming habit of the plant epiderm, and what makes the likeness more striking, is that the exudate is practically identical with the serum, which "skins over" an abrasion or scratch in the process of repair, and that it has high germicidal powers, as has been proved where the blebs were large enough to permit of its collection in adequate amounts. It is due to precisely the same sort of causes, for all dermatologists are practically agreed that it is a dermatitis provoked by an irritant, *either external* or *internal*, or a combination of both. Its localization also corresponds closely, for its commonest sites are the areas of greatest exposure (the face, neck, hands and wrists), and the regions of skin which are thinnest, moistest, warmest, and most liable to friction against each other, soiling by excretions or accumulation of dirt, the flexor surfaces, and the folds under the breast, in the axilla and between the buttocks or thighs. The delicate, highly vascular skin of the child is also much more subject to its attack than the tougher coating of the adult. Even the form which it assumes depends largely upon the mechanical texture of the locality; eczema of the palms, nape, and back, is nearly sure to be papular and scaly; eczema of the eyelids, neck, or groins, vesicular or pustular.

Eczema in the other mammals is almost universally pustular and mycotic, because the hairy coating, while excluding irritation by temperature, moisture, or friction, affords abundant "cover" for parasites, whose highly irritating activities lift the process to the pustular stage almost at once. The pig, the Mexican hairless dog, and the elephant, suffer also from the papular and scaly forms. In short, eczema would appear to be one of the forms of the great "exudation reflex" of living matter, the commonest and easiest response which the skin can make to the undue pressure of its environment.

Eczema is extremely common in the domestic animals, and nearly 90 per cent. of it is parasitic. It may be divided into three great classes, according to the organism incriminated, the mycotic, the sarcoptic and the insectal. The disease is comparatively rare in birds, whose feathers are probably a more complete protection to, combined with free ventilation of, the skin, than any other covering yet devised.

Simple or acute eczema is commonest in horses and dogs, chiefly beginning along the spine, at the back of the ears, or at the root of the tail. It may be caused by the pressure of dirty harness, too close clipping of the coat, mycosis, and the bites of insects with the scratching they give rise to. It is very troublesome upon the ears of dogs kept on the chain in hot weather. The ear feels hot and swollen to the hand, and its inner surface is studded with a crop of firm papules, which give a distinct "shotty" feeling to the skin.

If neglected it may develop into the chronic form, choosing usually the favourite site of attack in our own species, the flexor surfaces. If it attacks the back of the fetlocks in the horse, it forms the familiar "grease," if the hock or stifle-folds, it is termed "mallanders."

Although usually of external origin, it may also be caused by errors in diet or other internal causes, like our "gouty" and "food" eczemas.

"Grease" in the horse is often the result of over-feeding, while a severe form of the disease occurs in oxen from eating mouldy fodder or distillery waste. This is especially apt to occur where potatoes are used in making the "mash," and either the waste-pulp or the undersized tubers given to the cattle, hence the disease has been termed "malt-eczema." It may have a mortality of from 5 per cent. to 20 per cent., and is variously regarded as due to poisoning by waste alcohol or by solanin, the alkaloid present in "green" potatoes.

Eczema also occurs, though rarely, in the pig, in whom it is due to insanitary pens, bad food, or exposure to cold, wet weather, or to a combination of all three. It is a disease of marked severity, which not rarely proves fatal.

Urticaria, though rare in these animals, may be seen upon the skin of the horse, the dog, and the pig. Large and well-marked wheals appear, and their eruption is attended by great irritation, nervousness, and a distinct rise of temperature. As in ourselves, gastric disturbances usually underlie the outbreak.

A very curious form of *gangrenous dermatitis*, attacking only the *white* patches in piebald animals, occurs in both cattle and horses. It seems to follow prolonged exposure to the sun's rays, and may throw some light upon the advantage of pigment in the human skin in tropical climates. The entire thickness of the skin becomes gangrenous and sloughs in patches of the size of the hand. The animals may be in perfect health, and we have absolutely no clue as to its causation.*

Pemphigus and *Alopecia areata* may also be found, the latter in the dog, but both are rare. As for the parasitic

* If we except the suggestion of Blake, that it is due to over-stimulation by light, a sort of *eczema solare*. Compare the sloughing caused by electricity and by Röntgen rays.

diseases other than eczema, their name is legion. *Ringworm* is fairly common in calves and lambs, where it is known as "thrush," and it may also occur in puppies. *Favus* also attacks various mammals, especially mice, but is commonest in poultry.

Of the *Manges*, there are three great groups, each of which includes four or five species of acari: the *Sarcoptic*, attacking chiefly the denuded regions of the body; the *Psoroptic*, invading the hair-covered areas of the trunk; and the *Symbiotic*, chiefly confined to the extremities. Of these only the Sarcoptic group is readily transmissible to man. Like most widespread diseases of the animal skin, they may produce grave constitutional effects, and some epidemics of them have a considerable mortality, especially in dogs and foxes. Sarcoptic mange is said to constitute nearly 10 per cent. of all diseases in the dog.

Psoroptic mange is very prevalent among sheep, forming the familiar "scab," for which dipping in sulphur lotions or tobacco-water is resorted to, although this must not be confused with a much graver disease known by the same name, the ovine form of small-pox.

Birds seem to be singularly free from all forms of skin disease, with the exception of those due to acari, fleas, and other animal parasites. In over one hundred autopsies upon representatives of almost every order, I have found extremely few dermatological disturbances, even of parasitic origin, although fleas and lice are fairly common. About a third of the birds dying in captivity are in bad feather, due to imperfections in the moulting process, which may be produced by any form of chronic wasting disease, especially tuberculosis. Indeed, most poultry-keepers regard a "bad moult" as almost pathognomonic of the last disease. It may, however, be produced by any cause which seriously lowers the nutrition of the general system, and may either delay the shedding of the old feathers (some birds when first brought into captivity going nearly two years without a moult) or the coming in of the new. The disturbance produces not only a most dilapidated appearance, but also an aggravation of the morbid condition and much discomfort, as birds suffering from it are always depressed and inclined to mope. A form of "alopecia," due to eating each other's feathers, is not uncommon in poultry, especially when over-crowded, or insufficiently supplied with green food and meat or insects.

In Acne we have a disturbance so distinctly reversive in its nature, that it is hardly necessary to go outside of the embryology and pathology of our own species to prove its character, and the evidence is so abundant and so familiar to my readers that a mere *résumé* of it, is all that is needed or desirable here. Comparative biologists are practically agreed, (1) that man is but recently descended from a completely hair-covered ancestor; (2) that the nearly complete denudation which has taken place, has been brought about in response to his standards of beauty, and not by the substitution of clothing as a protection; (3) that this denudation is *nowhere complete*, hence the nakedness of any part of the skin is simply relative; and (4) that the so-called "sebaceous" glands are solely and exclusively appendages of the hair follicles, so that their presence invariably denotes either the present or former existence of hair in that region.

The first and fourth propositions need no defence, but in regard to the influence of ideas of beauty or ornament in bringing about this change, it may perhaps be suggested, first, that this change invariably begins among the primates upon the face (except in certain Apes, where by a strange freak of taste, it is upon the buttocks), and in the human species is most constant and complete in this region, which is the chief criterion of beauty for the entire body (hairiness of the arms and chest, for instance, is three times as common as that of the face). Second, that substitution by clothing is entirely inadequate, for scores of savage tribes can be found whose skin is as completely denuded as our own, and whose only clothing is a breech-cloth. Third, that the hair has been permitted to remain in only those places where it either never showed, as in the axillæ and about the pubes and perineum, or where it was regarded as an ornament, upon the scalp in both sexes, and upon the jaws and lips of the male. In both of which latter situations it has been developed almost into a neomorph, an appendage without parallel elsewhere in the animal kingdom, save in some monkeys, the goat, and a few deer and antelopes.

As to its incompleteness, a careful examination with the naked eye or a weak lens will soon show that, with the exception of the eyelids, penis, palms, and soles (and even here the "sebaceous" hair-glands are still present), the nakedness of any region is simply a question of the sparseness, fineness, and whiteness of the hairs which cover it. More convincing, however, is the test of exposing the surface to a cold draught, and watching the "goose-skin" develop over every inch of it, which of course is the involuntary action of the *arrectores pilarum*, pulling up the mouths of our hair follicles, in the effort to erect our hairy coat, as they used to do in bygone days, and as other mammals do now when chilled. In the embryo the lanugo coat covers the entire surface, and is often so dense as almost to suggest fur.

But what has this universal hair-distribution to do with acne? In the first place, it is primarily and almost throughout a disease of the so-called sebaceous glands; in other words, of the immature or aborted hair follicles. In the second place, it usually makes its first appearance at one of two periods in life, most commonly between the ages of fifteen and twenty, and less so between forty and fifty, especially in females. Now, is there any normal special tension in any part of the hair coat at about these periods? The coincidence in the first is most obvious, for this is the period of puberty, at which a powerful growth-impulse, what the old transcendental naturalists called a "*nisus formativus*," is set up in the hair follicles of certain regions, by which the lips, chin, chest, arms, and pubes in the male, and the last only in the female, become covered more or less profusely with hair, one of our most marked secondary sexual characters.

We can hardly imagine this surging impulse limited strictly to these small and irregular tracts of the great hair coat, and we cannot be in the least surprised to find all the hair follicles upon the body, and especially those along the borders of these pubertal regions, sympathizing with it. With some it is only the flow of blood into their embracing mesh that is increased; in others the secretion (sebum) of their lubricating glands is increased; in others the stunted hair shaft makes an attempt at growth, but twists upon itself, bruises the sides of the follicle, even grows into the mouth of the lubricating gland. Neither hair nor sebum can escape through the contracted mouth of the follicle, a plug of hair and sebaceous detritus packs its cavity tightly, back pressure is set up, the gland ducts become distended, the outer end of the plug becomes soiled and septic, strepto- or staphylo-organisms lodge upon it and penetrate into the gland, turn its contents to pus, and set up local inflammatory processes all around it, and behold, an acne pustule.

In many of them, the stunted or twisted hair can be actually demonstrated, but in most the impulse seems to go no further than the production of superfluous and functionless sebum, which dries down into the familiar comedo, or "face-worm," until it can be either pressed out or absorbed. And this process usually begins, and in most cases is confined, to that region which borders the growth area, and is exposed to the atmosphere, the face. The universality of the disturbance well-nigh stamps it as a process of nature, or in some way related to one, for while only a moderate percentage of the human family develops acne, nearly everyone suffers from "pimples" or "a bad complexion" at some time during this pubertal period, and as certainly recovers from it when the wave of sexual development has been merged in the full tide of maturity. Whether this shall develop into acne seems chiefly to depend upon the presence of either an unusually thick, firm, "greasy" epiderm, or a thin, fine skin, easily irritated, or readily setting up pus formation—the "strumous diathesis" of our ancestors—or, far more commonly, an intestinal toxæmia with consequent attempts at vicarious execretion by the skin. Hence the sovereign value in acne of hot soapsuds, laxatives, and time, particularly the last.

"But," says someone, "even if this apparent connection be a genuine one, this would only account for the occurrence of acne in the male." To this we would reply, first, that this process is decidedly commoner in the male sex, although on account of the much greater sensitiveness of girls and young women to anything which disfigures the complexion, the number of *recorded* cases is almost the same for both sexes. One seldom sees a really "furious" case of acne in a female. And, secondly, that so completely does each sex contain all the possibilities of the other, from clitoris to *uterus masculinus*, that even secondary sexual characters belonging to the opposite sex may be more or less imperfectly developed, and there would be nothing at all improbable in the follicles of the female face region sympathizing with the general pubertal hair growth.

As a matter of fact, a considerable proportion of women will be found to have a distinctly heavier coating of downy hairs upon the upper lip than upon the rest of the face, which preponderance dates from puberty. Indeed, this sympathy is shown in a curiously inverted fashion later in life, after the menopause, when the facial hairs being, as it were, released from the domination of the distinctively feminine element, in some cases suddenly begin to grow and develop into unsightly tufts upon the skin, and streaks upon the upper lip, especially in nulliparæ and old maids. And by, at the least, a singular coincidence, it is precisely at this period, in this region, and in this sex and condition, that the second outburst of acne is most liable to occur.

Note that it is not the follicles which are fully "functional," or even have such possibilities in them, which are attacked, but the atrophied and "functionless" ones. Acne never attacks the continually hair-covered regions of the body, the scalp and eyebrows, and seldom those regions which are uniformly, or generally clothed with even downy hair in both sexes sooner or later, as the pubes, the axilla, and the upper lip, but only the denuded portions of the body, and by far the most frequently, the most completely and uniformly denuded portion of all, the face.

We have also a valuable piece of negative evidence in the fact that in none of the other mammals with their uniformly hair-covered surface is any similar, or even related disease to be found. With the exception of a few pimples containing sebum which occur upon the *nearly denuded* skin upon the muzzle of the horse, or round the nostrils of the dog, and thus conform to our suggestions. The so-called "contagious acne" of the horse is an infectious, pustular eruption, allied to impetigo. This extreme rarity in animals is almost inexplicable in a disease of the hair follicles, unless denudation and atrophy play the chief part in its causation.

To sum up, my contention is (1) that acne is a disease exclusively of the hair follicle and its appendages; (2) that it attacks only those which are more or less atrophied; (3) that this attack is much more liable to occur at certain periods, viz., the years of, and those immediately succeeding puberty, and those of the menopause; (4) that this liability is due to the growth impulse which at these periods normally affects the sexual hairs and radiates into the adjoining regions. Though, of course, these follicles, like any other structure in the body, may become attacked both by external infections and irritations, and in internal toxæmic conditions.

There is another skin disease, though a rare one, which has a distinct ancestral basis, without which it is absolutely incomprehensible, and that is Ichthyosis. This singular condition, which has attracted marked attention from the earliest periods of medical observation, is always congenital, or appears during the earliest years of life, tends to be hereditary, and is absolutely unaffected by treatment, except such purely mechanical methods as constant lubrication or wearing down the keratin with sand-soap. The meaning and origin of this singular keratin-forming tendency on the part of streaks of the epiderm was a total puzzle until the ingenious researches of Bowen and Ohmann-Dumesnil proved it to be the persistence of the *epitrichium*, the parchment-like outermost layer of the skin in the embryo, under which the hairs and sweat-glands are formed, and which normally breaks down at about the fourth month, and assists to form the *vernix caseosa*. This discovery would also account for the absence of perspiration and consequent distressing dryness and fissuring of the affected areas. And when we remember that the earliest appearance of hairs in mammals was at the base and under-surface of scales, the conclusion draws itself that the human embryo is primarily covered by precisely the same keratogenous layer of epiderm as its piscine, reptilian, or chelonian ancestors, which, however, instead of developing into scales or "shell,' is normally shed after the hair and sweat-follicles have been formed beneath it. Except in those fortunately rare cases in which it persists, to produce the rough, shagreen-like skin of ichthyosis—an ancient medical term which, for once, happens to mean something rational, but of course by accident.

A most striking illustration of the relation of the horny tissue in ichthyosis to the hairs may be seen in cases of the disease in animals. Here the stiffer hairs force their way out under and behind the broad scales and bands of horn, so that they give the animal a most curiously armadillo-like appearance; in fact, they reproduce a curiously close imitation of the condition under which hairs originally appeared in the ancestors of the mammals. There is in the museum at the Royal Veterinary College, Camden Town, a stuffed specimen of a young pig, which is almost completely "armoured" with broad encircling scales and plates, from under the edges of which thick tufts of bristles grow out, and in places seem to lift the plates away from the skin. Whether in infantile pemphigus, a disease again congenital, of unknown origin, and most intractable, all of whose known pathology might be summed up in the sentence that the horny layer of the epiderm *will not* "stay on," or as Jonathan Hutchinson has expressed it, "a skin that does not wear well," but floats up all over in blebs, which rapidly turn into bullæ—whether here we have another tendency to revert to the unstable amphibian epithelium (salamander, toad) would, be impossible to say in the present state of our knowledge; and even the suggestion of such an origin is of the wildest.

Finally, the external portion of the great skin sheet shows a close and prompt sympathy with the troubles of everyone of its descendants however remote. With the kidneys (as will be discussed later), the lungs, the stomach, as in the numerous "food eczemas," and the extraordinary vagary of urticaria, a disease in which the stomach disturbance literally photographs itself upon the skin, where the alimentary canal turns over, as it were, its case to the skin for presentation. In many cases the eruption will appear abundantly upon the skin before the offending morsel has been in the stomach twenty minutes, long before any absorption can have taken place, and even before the gastric mucosa has telegraphed its uneasiness to head-quarters. The skin literally makes the stomach's protest for it, and so vigorously does it take up the quarrel of its blood relative that the latter has frequently no need to pursue the matter further. And the same close "primæval sympathy" registers itself upon the epiderm of our dietetic first cousins, the pig and the pug-dog.

Even with that far-wandered strip of the ectoderm, the brain-cord, some curious family relations are still maintained. The singular flushes and eruptions which accompany cerebral and meningeal disturbances, the agonizing pustules of zoster, the glossy varnish of scleroderma, the *tache cérébrale* illustrate the old blood-tie.

And even between their functional activities the tie yet holds. A leading American dermatologist has recently thought it worth while to devote an entire paper to the consideration of "Sleep in Diseases of the Skin," in which he convincingly shows the close and singular relation which exists between chronic disturbances of the skin, especially eczema, and the power of sleeping. A very considerable proportion of all his patients having an eczema of any considerable extent of area and length of duration, are annoyed by insomnia, which promptly subsides or increases *pari passu* with the skin affection.

So constant an index is it that lessening of it will be one of the first signs of improvement, even before any change can be detected in the skin, and Bulkley says that he has got into the habit of enquiring for and depending upon it as one of the most reliable indications of progress. In severe and wide-spread eczemas, it becomes one of the most serious complications, and may even lead to a fatal result. He declares that neither itching, mal-nutrition, nor any other symptom is at all adequate to explain this reflex, and the only way of accounting for it is by supposing the existence of a singular sort of sympathy between the skin and the brain cortex.

Bulkley is also inclined to regard a similar factor as underlying that wide-spread tendency of all sorts of itching eruptions to become worse at night, just as the cortex is beginning its automatic vagaries. Night-itching would appear to be a sort of dreaming on the part of the skin, an aimless flashing hither and thither of swollen rumours of half-imaginary irritations, when the stern control of cerebral inhibition is withdrawn. Like any other specialist, the dermatologist must be constantly alive to the fact that, mingled with the simple pictographs of external irritation or purely dermal disease, will continually be found the "hand-writing on the wall" of any and all of the buried roots of the great epidermal family tree. Here, as everywhere else, a thorough working knowledge of general medicine is absolutely necessary for successful, ration a specialisation. This point of view removes for ever the reproach, applied to the dermatologist, of being a mere "skin doctor" or a complexion improver. And the most notable service to modern medicine of the distinguished writer above quoted, has been his insistence upon and brilliant exemplification of this broad, rational, well-balanced view of the problems of his specialty, based upon a thorough preliminary knowledge of all the underlying factors.

The Kidneys.

In considering the diseases of the kidneys, from a comparative point of view, the chief interest centres about their double origin. For an organ that has varied so greatly in both position and external form, the internal structure of the kidney has been singularly similar through all the ages. Beginning with the pair of coiled epithelial tubules (nephridia) in each segment of the earth-worm, each opening from the peritoneal cavity (cœlom) to the exterior, and the thirteenth pair transmitting the genital products, through the loosely-clustered coil-groups of the mollusca, the ragged and indefinite string-of-beads-like organ, moulded into the depressions along each side of the centra of the vertebral column of fishes, to the compact, definite, rounded kidney of the bird and mammal, the essential ground-plan has been strikingly uniform. Just a group of fine, many-coiled tubules, sucking the nitrogenous waste first (Vermes) directly out of the body-fluid in the cœlom and tissue-spaces, later out of a fine-meshed, curled-up knot of blood-vessels which thrusts itself into the grasp of the primary coil, and coils round their lower part in turn.

Whether they are deployed in double file almost the entire length of the body, as in the worm, or drawn up in irregular columns of four, along the body-cavity, as in the fish, or concentrated in the lumbar region and formed into compact, hollow squares, as in birds, is simply a matter of convenience. The skin-coil and the blood-coil in their mutual embrace are one and the same all through. Similarly, it is merely a question of executive administration whether each tube open separately upon the surface, or all upon one side into a common gutter of the skin running lengthwise as regards the body, or into a tube formed by the "sinking-in" of this gutter, which, at its union with its fellow of the other side, forms a cess-pool, first opened and later closed, known as the bladder. Only the knot and the coil are fundamentally essential. These two, having such widely different origins, yet have corresponding sympathies. For many years past, clinicians have divided diseases of the kidneys into two great classes, the parenchymatous and the interstitial, the epithelial and the vascular. The two groups are sharply distinguished from each other in point of attack, causation and history, though either, of course, may ultimately involve the other, and also the patient. The relations of the first group are unmistakably with the epithelial surfaces, especially the skin, as in the nephritis of chill or exposure, of burns or of scarlet-fever. The connections of the second are equally close with disturbances of the vascular system, as in chronic Bright's disease, in the syphilitic, and the "gin-drinker's" kidney. In fact, the first of these latter is now regarded as simply a local and focal manifestation of a general arterio-capillary fibrosis. The same division and distinct relations are found in the renal diseases of dogs, horses, and cattle.

Why the two essential elements of the organ should manifest such widely different sympathies was a decided puzzle, especially as embryologists assured us that the entire kidney was derived from the mesoblast. Gradually, however, this statement came to be more and more questioned until of late the researches of Van Wijhe and Rückert have practically settled that the Wolffian duct, and the tubules of the permanent kidney (Metanephros) are derived from the ectoderm, and only the vascular portion (glomeruli, etc.) from the mesoblast.

Here again, as often elsewhere, the "scent" of the clinician was truer than that of the laboratory-worker, and pathological evidence pointed more clearly in the right direction than embryological. The sympathy of the uriniferous tubules and capsules with the great skin-sheet, and of the glomeruli with the blood-vascular system, is a sympathy due to community of descent. Even histologically, the likeness between the *tubuli contorti* and the coils of the sweat-glands is a striking one, and their function to-day differs only in degree and molecular proportions of product. The promptness and efficiency with which either will do substitute duty for the other is one of the most familiar facts in practical medicine, and one of the most frequently appealed to.

Nor is this merely in their drainage action, as in the familiar increased flow of urine upon a cold day and diminution upon a hot one, but upon occasion the simple coil-glands can duplicate even the metabolism of their highly specialized inland cousins in the renal cortex. The sweat becomes not merely profuse, in uræmia and puerperal convulsions, but also loaded with urea, made, not in the blood, but in the coil-glands. In typhoid fever the perspiration is as loaded with toxic materials as the scanty urine. Some crude attempt at vicarious excretion would appear to be a factor in the obstinacy of certain eczemas in renal inadequacy and gout.

In short, the skin which originally gave birth to the permanent kidney can still give rise to a temporary one upon emergency.

Patients with serious renal inadequacy can now be kept alive and in fair health for years by the systematic hot bath and hydragogue laxative. Simply making two descendants of the great skin-sheet do substitute-duty for a third.

The chapter upon diseases of the kidney is confessedly one of the most unsatisfactory in veterinary pathology. This is due chiefly to the small use yet made of analysis of the urine as a routine procedure in veterinary practice. The difficulties in the way of this are far greater than in our own species. First of all, it is always difficult, and in some cases impossible, to collect a sufficient quantity of urine, as the volition of the animal cannot of course be brought into play. Then, the quantity of salts in nearly all animal urines is so great as to seriously interfere with the chemical tests—alkaline earthy phosphates in herbivora, and sulphates and chlorides in carnivora. Herbivorous urine is often so thick and turbid as to mask the more delicate reactions; we have seen the urine of horses so loaded with earthy phosphates and carbonates as to resemble a mixture of urine and white-wash, leaving chalky stains upon everything it splashed upon. Then, also, the trace of albumen, normal in human urine, is often present in larger quantity in the herbivora, especially in hard-worked horses; and in the ox and sheep traces of sugar are normally present.

After allowing for these obstacles to diagnosis and recognition, however, there seems little doubt that renal disease is distinctly less common in the lower mammals than in our own species. Especially is this true of the chronic forms, which are decidedly rare. When such disturbances occur, they are due to similar causes to our own, and take nearly identical forms. Acute nephritis, for instance, which occurs in horses, dogs, and oxen, may be due to a chill, a violent strain, or great nervous excitement, but is more commonly a result of infection, as in the exanthemata, or of mouldy or fermenting fodder or grain. Chronic nephritis may be due to similar causes, and is usually of the parenchymatous type, the "large white kidney" being more common than the granular contracted form, though neither is at all frequently found.

In some hundred and fifty autopsies upon mammals at the Zoo, I attended especially to the condition of the kidneys, and found only two cases of large white kidney and one of the contracted form. Indeed, renal lesions appreciable by the eye were decidedly rare. I found three cases of multiple cysts of the cortex of moderate size, in a badger, a monkey, and an agouti, all apparently of parasitic origin. Sections of the last, kindly prepared by Dr. Foulerton, showed the smaller cavities filled with rounded, apparently nucleated, coccidia-like bodies, though Dr. Rolleston, who also examined them, was inclined to regard them as cell degenerations.

Slight degrees of both anæmia and congestion were occasionally found; in three cases there were hæmorrhagic streaks, and in one a few small infarcts in the kidney substance. Nodules were present in five cases of general tuberculosis, but these were generally superficial, or involved only small amounts of the cortex. Both kidneys of a prairie dog were packed and swollen with masses of new-growth, apparently sarcomatous, but which proved of such anomalous structure under the microscope as to completely puzzle us, and render definite identification impossible.

In only one case was purulent nephritis or pyelitis found, and that was in a polar bear, in which a violent suppurative process in one kidney, attended by free formation of gasbubbles under the capsule, and resulting in general septicæmia appeared to be the cause of death. In the great majority of cases, however, the kidney substance was clear, fresh-coloured and glistening on section, and a thickened or adherent capsule was a rarity.

In birds, recognizable renal lesions were even less frequent, but we know so little of the appearance of and changes in their kidneys, in either health or disease, that this fact proves little either one way or the other.

True uræmia is, from some cause, extremely rare in animals, either in acute or chronic nephritic processes. The only exception is the dog, in whom both coma and convulsions of characteristic type occasionally occur, usually in consequence of the obstruction of the ureter by renal calculi or from paralysis of the bladder. I have seen one such case through the kindness of Dr. Martin of Buffalo, in an old pointer, who had a number of uræmic attacks, beginning with suppression of urine, vomiting and convulsions, and ending in profuse diarrhœa. The symptoms pointed strongly to renal calculus. Dr. Martin also reported a similar case to me in which, at the autopsy, a stone was found impacted in the prostatic portion of the urethra, and both kidneys had undergone cystic degeneration. Fatal attacks of typical eclampsia are not uncommon in nursing bitches. Damman has reported a case of uræmic convulsions in a sheep, and Pflug in a cow.

There is one disease whose symptoms strongly suggest uræmia, and that is the puerperal paralysis of cows. This usually begins a few days after parturition, with slight convulsions, followed by coma rapidly deepening into paralytic collapse. Albumen is often present in the urine, the temperature, at first high, becomes sub-normal before death; the brain is often œdematous, but no alterations have yet been discovered in the kidneys. I made an autopsy upon a case of this disease in the practice of Dr. Martin, but could find nothing abnormal in the viscera and no albumen in the urine retained in the bladder.

Although in no sense a disease of the kidney, it may be of interest to note that diabetes mellitus occurs occasionally in the dog and very rarely in the horse. U. Le Blanc has reported a case in an ape. The symptoms are strikingly similar to those in the human form,—thirst, emaciation, polyuria, cataract and corneal ulcers, and its course is equally fatal. Nor is excess of sugar in the tissue fluids confined to the animal kingdom, plants also suffer from it. Galloway has reported an epidemic among hot-house violets, due to an excess of sugar in their tissues, which rendered them liable to the attack of bacteria, producing a rapid form of "moist rot."

CHAPTER IX.

The Biology of Tumours.

In the process of tumour-formation we find one of the most puzzling, and yet most fascinating, problems of pathology —a process, the intensity of whose interest can only be adequately characterized by the term "dramatic"—dramatic alike in its essential character and in its tragic possibilities.

The principle of development of a tumour is a biologic anomaly. Everywhere else in the cell state we have found every organ or part strictly subordinated in both metabolism and structure to the interests of the whole. Here this relation is absolutely disregarded. In the cell-republic, where we have come to regard harmony and loyalty as the almost invariable rule, we suddenly find ourselves confronted by anarchy and rebellion.

And yet, after all, there is nothing to greatly surprise us in this. It is true, that upon the basis of an endless series of experiences, almost monotonous in their constancy and similarity, we have come to reckon upon this subordination of the cell to the tissue, the tissue to the organ, and the organ to the organism, as one of the most firmly-grounded laws and most abundantly attested facts of nature. But this subordination is very far from a mere automatic or mechanical one, like the cog in the machine or the brick in the wall. It involves not only a high degree of vitality and complexity of metabolism, but often of initiative and independence as well. The ingesting powers of the alimentary, the selective ones of the renal epithelium, the contractility of the neurons, will at once suggest themselves. These have been discussed in a previous chapter. Indeed, upon *a priori* grounds, the wonder rather is that, such a degree of individual attainment and activity being necessary, the line of usefulness to the organism is not more frequently overstepped: not that tumours occur, but that they do not occur far oftener.

First of all, of course, it is necessary to endeavour to define what constitutes a tumour. The utmost we can hope for is a sort of working concept, sufficiently clear for the purposes of this discussion. As the best intellect of the profession has been struggling with this very question of definition for the past 200 years, and reached no better solution, as yet, than was indicated by Virchow's despairing outburst, thirty years ago, that "no living human being can define, even under torture, just what a tumour really is!"—

it would be presumption to hope for any more conclusive result.

For the purposes of this discussion, that is, from a biological point of view, we shall define a tumour as a localized cell multiplication which in no way subserves the interests of the organism. I am fully aware that this definition is probably open to as many objections as any of its predecessors, especially as to the teleological element involved in it, but I believe that it embodies, perhaps as nearly as any single phrase can, what I might term the essence of the tumour process. Any definition which is to be of the slightest practical value, either clinically or biologically, must recognize this independent, and at times antagonistic, element in the character of the growth.

Indeed, it will be found to be included in most of the classical definitions, one of the best and most modern of which, from the pathological standpoint, that of Thoma, for instance, gives it as an "*autonomous or independent* new growth"; and similarly eminent from the surgical point of view, that of Roswell Park, "a new formation not of inflammatory origin, viz., not due to the presence of, as yet, recognized and determined parasitic agents, characterized by more or less histological conformity to the tissue in which it has originated, *and having no physiological function*."

At first sight, it might appear that this definition would include those new growths, which Virchow classed as tumours in his superb and epoch-making "*Krankhaften Geschwülste*," under the title of "Granulomata," namely, tubercle and gumma. These, of course, are now recognized as mere reactions to infection, and, as such, eliminated from the tumour division in most classifications. And, as from the comparative point of view, we are coming to regard all such reactions as in their essence either protective or conservative, they will also be excluded by our working definition: as they thus subserve the interests of the organism.

In tubercle, at least, the proof of their conservative nature amounts almost to a demonstration, as the only known method of healing in this disease is by the successful inclusion of the attacking bacilli within the mass of fibrous, or, later, calcareous tissue resulting therefrom. Bacilli may be found, not only alive, but virulent in the centre of such scar-masses, months, or even years, after complete apparent recovery from the disease; and some of the most unfortunate results from the injection of tuberculin are ascribed to its action in breaking down these fibrous barriers and setting free the still virulent bacilli in the system. As Biggs has recently shown, cultures taken from the centre of fibrous, or even calcareous masses found at the apices of the lungs of those dying of other diseases, have proved fatal to rabbits and mice.

Certain it is, that the mere resumption of ancestral reproductive powers on the part of a group of cells, resulting in that local increase in bulk which is signalized by all the names which have been applied to the process, whether the Latin "*tumor*," the French "*tumeur*," the German "*Geschwülst*," or our vernacular "*swelling*," although it will invariably produce a "tumour" in this sense, by no means alone suffices to constitute what we mean by the present use of the term. This power of rapid "emergency" self-multiplication is, of course, equally well displayed in physiological hypertrophy, as of the uterus and heart, and in the last stages of the process of repair.

Nor can we be guided in any way by the fact that the cells thus reproducing themselves, do or do not "breed true," as fanciers say, for in the great majority of forms of the true tumours, the so-called "new growths," being then cells may be structurally perfect in almost every detail, as in lipoma and myoma, or even form themselves into true organs, as in glandular adenoma; the new tissue, in fact, being normal in every respect, except in the single regard of its relation to the rest of the body. By every histologic or chemical test which can be applied to it, the tissue of a fatty tumour is indistinguishable from any other portion of fatty tissue in the body; and only by the application of the physiologic test, as to whether it in any way responds to the starvation needs of the rest of the body, is its real character to be discovered.

Nor is, to my mind, the element of causation, which is included in so many of the definitions, a legitimate distinction, inasmuch as it simply amounts to the statement that this group consists only of those new growths whose causation is unknown, thus making our ignorance a basis of classification.

One of the chief objections to our basis of definition is that we come perilously near using not merely a teleological, but even a psychic or volitional characteristic as a means of physical classification; and yet this error is only apparent, for, while we must admit that, the more carefully we study these extraordinary phenomena, the more sorely tempted we are to impute an element of volition and even purpose to the cells concerned, and the tersest and most graphic, as well as most accurately characteristic definition of cancer which has ever yet been given, is the metaphoric one of Jonathan Hutchinson—" a rebellion of the cells." Yet upon a purely physical basis there is no fact more firmly supported by the overwhelming mass of clinical experience, and more readily demonstrable by fresh experiment at any time, than that these new growths which we call tumours do not, in any way, subserve or respond to the interests of the organism in which they occur. And while, of course, it is in the strict sense inadmissible to use terms implying psychic processes or concepts in the discussion and classification of physical phenomena, yet, as metaphors and illustrations, they are not only permissible, but often of the greatest value in enabling us to express what might be termed the soul of the process in not merely briefer and more graphic phrase, but even with greater clearness and scientific accuracy than is attainable by any other means. The value of an intelligent use of the imagination in pursuing scientific problems has hardly yet been recognized as it deserves, although it has proved a very guiding star of scientific progress in all ages, from the superb visions of Galileo to that masterpiece of the creative imagination—the Darwinian hypothesis. Even the celebrated phrase "natural selection" is a pure metaphor, and open to the grave technical objection of implying precisely this purposive or intentional element, a choice or expression of preference upon the part of nature; and yet what other phrase can compare with it in conveying a vivid and accurate impression of the essential nature of the process described?

And, while it would be unwarranted, if not absurd, to attach any idea of purpose to the cells concerned, either to serve the organism when forming a normal secretive gland, or to antagonize it in cancer growth, yet we believe that the very essence of tumour growth and character lies in the absence, not merely of any useful results, but of any tendency to produce the same. Any growth, which experience has shown to possess a tendency to subserve any useful purpose in the organism, such as callus or exudate, no matter how remote, or how often it may fail of its accomplishment, as tubercle, is not to be classed as a tumour.

From a biologic point of view, the most adequate working conception of a tumour is that of an organism within an organism; a new life-entity springing, it is true, from the cells of the body itself, but displaying as utter a disregard for the welfare of the rest of its tissues as any parasite from without. Its only connection with the rest of the body tissues is that it uses the latter as a source of food supply. Indeed, in completeness of independence, of uselessness, and even injuriousness to the rest of the tissues, it goes far beyond many of the entirely foreign organisms which have effected a lodgment. Large classes of pure parasites—indeed, from the rapidity with which their number is being added to every year, we might almost say, a majority of them—are found to enter into relations of, at least, mutual toleration and harmlessness with the tissues of their hosts, like the small fishes in the interior of the sea-cucumber (commensalism), or even of mutual advantage (symbiosis), such as the nitrifying organisms in the root tubercles of clover, and the bacteria in the alimentary canal of the herbivora, and possibly in our own food-tube.

Again, unlike parasitic relationship, there is absolutely no respondence nor correspondence, between its nutrition and that of the organism. No amount of overfeeding or healthy increase in weight on the part of the body will quicken the growth of even a lipoma in the slightest degree; nor, on the other hand, will any degree of starvation and emaciation diminish its bulk one ounce, or even check its growth. Indeed, as Bland Sutton has observed, the largest fatty tumours are usually found in patients otherwise thin and emaciated.

As to the relation to the surrounding tissues of their process of growth, nothing could be more absolutely indifferent. Whilst it is influenced by nothing save mere mechanical considerations, it moves ruthlessly in the direction of least resistance, whether this carry it toward the surface of the skin or into the yielding substance of the brain. And, even in its most benign forms, it will exert most injurious, and even fatal, pressure upon any tissue which may interfere with its expansion, whether it be bone, blood-vessel, nerve, air-passage, or food-tube.

Last, and most destructive of all, in every tumour of immature cell-type (malignant), and even in some of adult tissue-type, for many benign tumours show a strong tendency to become multiple, the new growth forms and gives off a sort of spore cells, which, carried by the lymph or blood currents to other parts of the body, may find a lodgment in the tissues, and proceed to reproduce, not a tumour of the type of the surrounding cells, but of that of the original neoplasm from which they were detached. A myeloid sarcoma of the thigh scatters its cells in the blood currents, and gives rise to other myeloid sarcomata in the lung or in the arm; a primary carcinoma of the rectum gives rise to secondary growths, each one of which absolutely reproduces the cylindrical cells and tubular glands of the rectal epithelium, alike in the centre of the liver and in the red marrow of the femur. Nor is this resemblance limited to structure only, for Stewart has recorded a most interesting case of disseminating cancer of the pancreas, in which the secondary growths in the liver and lung, not only closely mimicked the racemose glandular structure of the pancreas, but upon chemical examination yielded a high percentage of trypsin. This is one of the most extraordinary characteristics of cancer, of the highest significance from a zoological point of view, and one which, I think, is hardly appreciated at its full value in considering the causation of tumours. As Sutton says: "To find a tumour in the body of a vertebra, or in the shaft of the humerus, reproducing all the structural features of a rectal, thyroid or prostate gland, is one of the most surprising phenomena in the whole range of pathology."

This remarkable power of spore-formation, of bastard ovulation, would alone give it rank as an independent organism; and the more it is studied, the more incredible it appears that this faculty could be conferred upon any gland by the mere presence of a foreign germ, no matter how irritating. The parasite can be, at best, but the proverbial "last straw," or the spark which precipitates the explosion, although, of course, if future investigation shall prove that this outburst of independent proliferation does not occur except in the presence of such organisms, then these latter may be regarded as the cause of tumour in a most important and practical sense.

But this is as far as possible from demonstration, and the majority of pathological opinions at present strongly inclines towards Hansemann's statement that no proliferating stimulus, however vigorous, can produce a growth having these extraordinary powers of ovulation, unless it fall upon an abnormal, or, as he terms it, "anaplastic" cell.

The character of independent growth is a distinguishing characteristic of all tumours, but now the question arises, can we find any single biologic criterion by which we may distinguish between the two great classes of tumours, known crudely as the innocent and the malignant? This division is of course again open to the objection of classifying by results; but it has of course not only great practical advantage to recommend it, but will, we believe, be found to have a sound morphologic basis. The fundamental difference between them seems to be in the perfection of the neoplastic product.

If the cells of the new growth are in every structural respect the equal of the normal tissues from which they spring—in other words, if the form of the reproductive products be perfect and true to type—then the tumour may be clinically classed as innocent or benign. If the cells of the new growth, as a whole, or even in part, fall below the tissue from which they spring in perfection of structure—in other words, if the result of the reproductive process be imperfect structurally, the imitation incomplete—the growth will almost invariably display the clinical characters of malignancy. This position is practically supported by the conclusions, from a purely microscopic point of view, of Hansemann in his recent monograph, in which the degree of this failure to perfectly reproduce the type, or "anaplasia," as he terms it, is made the principal basis of his discussion and classification of malignant growths. I believe this distinction of the perfection of the product to be a fundamental and vital one, and to go far towards explaining the differing effects of these two tumour-groups upon the organism.

As a preliminary to further discussion, it is necessary to briefly consider the question of causation. Anyone who has paid the slightest attention to this phase of the subject knows that a mere enumeration of the theories proposed would fill a chapter in itself, and that any attempt at an exhaustive survey of this wide and wrathful field would require a separate monograph. Hence we shall attempt nothing farther than a brief survey of those few theories which have apparently proved themselves fittest by survival, and that only from the point of view of this work.

This may seem to be a brusque method of treatment, but it is, of course, all that is possible in the space at our disposal. In reality, many of the historic suggestions as to cause, such as diet, dyscrasia, perverted nerve-influence, etc., may be mentioned only to be dismissed.

Even the irritation, or injury, theory has been found, in the light of broader data, to depend chiefly upon the familiar confusion between *post hoc* and *propter hoc.* It would be difficult to find a starting-point for cancer upon or over which the patient could not remember to have received a blow, or injury, within the two or three years preceding its appearance; and, with the sole exceptions of the celebrated "chimney-sweep's cancer" of the scrotum, and "smoker's cancer" of the lower lip, irritation and trauma may be practically ruled out, as anything more than a hastening, or, possibly to some degree, localizing cause of tumour formation. And even in the last-mentioned instance, in view of the report of several cases in non-smokers (who, of course, form a very small proportion of the males in any community), its frequent occurrence in smokers of cigars or cigarettes, its appearance upon the opposite side of the mouth from that upon which the pipe is usually held, and often in the median line, and, finally, its occurrence, although with only about 1 per cent. of the male frequency, in women who have never smoked, and the fewness of reported cases in the "pipe" situation in old women who smoke (no inconsiderable number among the peasantry of Ireland, England and the Continent, as well as the remoter districts of the Southern South-Western States), the effect of irritation in causing even this form of cancer seems, on the whole, problematical.

On the other hand, three cases have been reported by Jonathan Hutchinson, in which the cancer recurred upon the opposite side of the lip, in the position to which the pipe had been shifted since the operation; and out of six cases in women reported by him, and one by Pemberton, four of the patients were smokers.

This, then, leaves four surviving theories of causation, some one of which is favoured by nearly every pathologist of prominence, and all of which are supported by such a body of evidence as to render it probable that each one plays an important part in the production of one or more classes of tumours. These are heredity, infection, Cohnheim's "rests," or vestigial theory, and what might be termed the evolutionary or "balance" theory, which regards tumours as arising out of the internal struggle for existence among the parts of the organism.

It will be seen at once that these theories are not mutually exclusive, that in many cases two or even three of these agencies may play a part in the production of a given tumour; and, indeed, with the exception of certain "infectionists," and possibly Cohnheim himself, no adherent of any one of these theories will venture to-day to claim that it is capable of accounting for all tumours to the exclusion of all other factors, although he might regard it as an underlying element in the production of a large majority.

As the sole purpose of this chapter is the presentation in this spirit of the last-mentioned hypothesis, I shall make no further apology for the brevity of my mention of the other theories, merely begging their adherents to believe that it is not intended in any sense as an indication of the relative importance which, in my opinion, is to be attached to them.

As to the influence of heredity as a cause of tumour formation, the evidence already upon record, although small in amount, is of such a peculiarly convincing nature as to leave little doubt that, in a certain percentage of cases, especially of cancer, it is to say the least a powerful predisposing cause. A number of instances are upon record by Paget, Bryant, Snow, and others, in which the disease has appeared in three and even four successive generations of the same family. Similar instances have probably come under the observation of most of us. In the family of a brother physician, a paternal aunt, father, and son, all died of cancer—the aunt and son of carcimona of the gall-bladder; the father, of epithelioma of the lip. A singular feature of this group was that the son died some five years before the appearance of the disease in the father.

In the family of a lady medical student, her grandmother, mother, two maternal aunts, and two sisters died of cancer. In four of these the carcinoma appeared in the uterus, and in two in the breast.

But, while this much must be admitted, it is equally incontestable that the percentage of cases in which this influence is at work is extremely small. In small series of cases we find a statement of a comparatively high percentage of this influence, such as Paget's—nearly 25 per cent. in 322 cases. Bryant, however, in 600 cases, discovers only 12 per cent.; Gross, in a slightly larger number, 9·7 per cent.; Sibley and Barker, 8·2 per cent. It will, moreover, be noticed that the more recent the investigation, and the larger the number of cases included, the smaller the proportion becomes. Some five years ago I succeeded in collecting a series of nearly 30,000 cases, in which hereditary history was present in only 10·5 per cent.; and when we further consider that by hereditary influence is simply meant the occurrence of a case of cancer anywhere in the family group of the patient within his own memory, or within that of his oldest living relative, and that the "related" tumours are often in totally different organs and in both sexes, we must admit that even of this small percentage only a few could be fairly regarded as influenced in any way by heredity.

Carcinoma is now known to be responsible for from 3 per cent. to 6 per cent. of all deaths over forty years of age; so that every family group containing twenty-five adults would, upon the law of averages, lose one member by cancer. In this instance, as, indeed, everywhere else, our use of the term "hereditary predisposition" is extremely vague, and is in need of vigorous overhauling and strict definition. From a biologic point of view, of course, the inheritance of characters which are not only of no advantage, but of distinct disadvantage to the organism, in its struggle for existence, is scarcely credible, or would be at best rigorously self-limited. Especially is this the case when we are considering a growth or character which by its very essence and definition is autonomous and *never becomes a part of the organism at all.* As a structure, we should have about as much ground for expecting the inheritance of a tapeworm as of a cancer. The utmost that could occur would be the transmission of a lack of resistance, or lack of balance upon the part of some particular organ, rendering it more liable to the setting up of the neoplastic process under strain or irritation. But this, of course, would require that the inherited tumour should appear in the same organ, a condition which is very rarely fulfilled.

One such instance, however, is historic; in the case of the Bonaparte family, four members of which, father, brother and two sisters of Napoleon, died, like the Emperor himself, of cancer of the stomach.

As to the transmission of innocent tumours, we have practically no evidence whatever.

There is, probably, no single problem in the pathologic world upon which more painstaking research has been expended than upon the infectious origin of cancer and sarcoma. Their superficial history and course so closely resemble that of an infection, their etiology would be so delightfully simplified, and, above all, the gloomy problem of their treatment, and prevention would be made so much more hopeful, that it is little wonder that the hopes of both investigators and operators should have turned strongly in the direction of a parasitic origin. Not only have we strong grounds in analogy for suspecting an infectious element in cancer, its close and unique resemblance to gumma, condyloma and tubercle, its formation of toxins which poison the lymph-stream, and its power of dissemination, but the position of the localities most frequently affected is extremely suggestive. It has a well marked preference for the orifices and sphincters of the various epithelial canals, such as the lips, the rectum, the cervix uteri, the breast, etc., precisely the regions which are most exposed to infection *viâ* skin, mucous membrane, or both.

Yet, it must in candour be admitted that the positive results of all this research have, so far, been most disappointing, either as to the identification of a causal organism, or as to the inoculability of either cancer or sarcoma. Not only is there no agreement among any considerable number of investigators as to the actual germ responsible, but there is a wide division of opinion as to whether it belongs to the vegetable or animal kingdom. The earlier investigators discovered bacterial organisms; the bulk of the modern ones, a coccidium or other sporozoon; the latest researches, such as those of Roncalli and San Felice, a yeast (myxomycete). With the exception, perhaps, of the last-named, very few of these discoveries have been able to stand the test of corroborative investigation, indeed, most investigators begin their own announcement by a destructive criticism of all preceding work and theories. Many of the proclaimed "cancer germs" have proved to be merely, in the words of Hansemann, in his recent masterly *résumé*, "degenerated cells, karyokinetic figures, white and red corpuscles, and, finally, normal carcinomatous cells"; and he speaks of the parasitic theory of origin as "already belonging to history."

Instances of successful inoculation of malignant growths from man upon animals are rare, but this weighs but little in the argument on account of the extreme rarity of cancer in the lower animals, and their apparent immunity to it. In short, we are compelled, however reluctantly, to admit with Schwartz, in his elaborate monograph, that the parasitic origin of cancer is entirely unproven as yet, although some extremely interesting results have lately been reached by Roncalli with his myxomycete, and the subject is worthy of the fullest and widest investigation, in the interests not merely of science, but of humanity.

It is of course obvious that, even should the parasite or parasites be discovered, and prove capable of conveying the disease, this would form but a partial explanation of the causation of tumours: first, because we have no reason whatever, either in analogy or evidence, to suspect an infectious origin in the innocent tumours—indeed, only a very few enthusiastic bacteriologists have even suggested it; and, secondly, because in view of the marked dependence of cancer upon the age of the individual and the history of the organ attacked, infection could at most be only one of the factors in its production. As Thoma remarks, after speaking of the "altogether questionable etiological importance" of the various parasites described, "without the intervention of other factors they would not suffice for the production of carcinoma, or carcinomata would occur with much greater frequency."*

The celebrated embryonal theory of Cohnheim is the most brilliant and attractive hypothesis as yet advanced to account for tumour formation. In a partial form, this view

* "General Pathology," 1896, p. 596.

dates from the investigations of Remak, and later of Virchow; and, as developed by Cohnheim, it claimed all tumours as springing from groups or "islands" of cells which, during embryonic life, had wandered from their normal position and surroundings into other tissues. These he termed "rests" or "residues," and declared to be the only true tumour germs.

This was of course far too sweeping a generalization, but it was a most brilliant one, especially in view of the fact that it was advanced upon the merest handful of the evidence which has now accumulated in its support. Its truth is now practically demonstrated in one great group of tumours, the dermoids, in many forms of cyst, and it is generally accepted as explaining the heterologous tumours, such as the non-sarcomatous chrondromata of the parotid or testicle, and probably certain of the homologous tumours, such as myoma of the uterus. It can, however, hardly be regarded as applicable to either sarcoma or cancer.

Last of all, the evolutionary theory holds that tumours are the result of disturbances of that balance which exists between all parts and tissues of a normal organism. The internal struggle for existence which goes on between the organs of a body and the cells of a tissue, just as it does between the individuals of a species, or a community, results in the success of certain groups of cells, and the placing of other groups at a disadvantage. Should this relation persist, these latter steadily diminish in size and vigour; the group, or organ atrophies, and may even entirely disappear. This is the usual result; but, if at any stage in this process the cells which have thus, as it were, been thrust out of the active life of the organism, when threatened by extinction, revert to their ancestral power of rapid multiplication by fission, then a tumour is born. This, it will be seen, includes Cohnheim's theory, as one of the methods by which this alienation from the service of the body, this disfranchisement, or outlawry of certain bands of the citizen cells may occur, viz., embryonic isolation.

But even this, in many cases, is simply the result of a similar process of elimination by struggle going on in embryonic life. The gill-clefts, the thyroid duct, the thymus, the post-anal gut, have all played their part in the economy of the organism, been worsted in the internal struggle for existence, and are dying-out in consequence. In 995 out of every 1000 human beings, first they atrophy, then they rapidly and completely disappear; in the remaining five they hold their own, and begin to multiply and grow upon their own account.

But, it is not necessary to suppose the presence of a cell-group detached during embryonic life; not only does this process of elimination go on all through childhood in whole organs, such as the thymus, the tonsils, and the patches of Peyer, but every cell in the body almost certainly becomes "detached" in this sense, sooner or later, dies, and is absorbed, unless it saves itself by rapid ancestral multiplication on its own account. It is not the occurrence of tumours which needs to be accounted for, but their infrequency. And the more primitive the cell, the more easily does it take on this independent multiplication; the frequency of a tumour is in direct proportion to the simplicity of the cells composing it. Fatty tumours are excessively common, true neuromata extremely rare, striped muscle tumours, unknown.

This hypothesis is advanced with much diffidence, and not as in any way an exclusive or complete explanation of tumour-formation, but simply in the hope of affording by its application a somewhat clearer and broader view of the real character of the process.

For the same purpose I shall suggest a classification based upon the cytologic properties of the growth, although claiming no superiority for it, except that it is most suitable for a consideration of the subject from this particular point of view.

Upon this basis, tumours may be divided into three great classes: those starting from cell-groups of adult type, or Tumours *par excellence*; those starting from cell-groups of embryonic type or Dermoids; and those of mechanical and obstructive origin, or Cysts. The first of these is again divided into those whose cells accurately reproduce the parent tissue, "successful imitations," as it were, or innocent tumours, and those whose cells fall short of this accurate reproduction, the malignant growths or "parodies."

I. *Starting* from *Cell-groups* of *Adult* Form:

- *a. Resemblance Perfect:*
  - 1.—Mesoblastic.
    - Lipoma, Fibroma, Myoma, etc.
  - 2.—Epithelial.
    - Adenoma, Papilloma, etc.
- *b. Resemblance Imperfect:*
  - 1.—Mesoblastic.
    - Sarcoma.
  - 2.—Epithelial.
    - Epithelioma, Carcinoma.

II.—*Starting* from *Cell-groups* of *Embryonic* Forms:

Dermoids.

III.—*Obstructive Tumours.*

Cysts.

Of these only the First Class claims our attention here, for the Second (Dermoids) is fully accounted for by Cohnheim's theory, while the right of the Third Class, of Cysts, to be included among tumours is of the most technical and formal character, and depends solely upon their singular power of continuing to add to their fluid contents, even after the glandular elements in their walls have been distended into parchment.

Even of the tumours proper, only such as are of special interest from a comparative point of view will be discussed, the others being merely mentioned, to indicate their place in the scheme of classification.

Beginning with the "imitation" division and the mesoblastic group, Fatty Tumours first claim our attention on account of their frequency and typical character. These are not only by far the most numerous group of innocent tumours, but as absolutely ubiquitous in the body as the tissues they spring from and imitate. They range from the conjunctiva to the sole of the foot, and from the dura mater to the peritoneum, but are by far most common in the two situations where fat is most abundant—the subcutaneous and subserous tissues, the two great storage regions of the body. It is also significant that this extreme frequency is coincident with, not merely the abundance of the fatty tissue in the body, but also the primitive character of the fat-cell. There is only one tissue in the body more primitive, less differentiated, and that is the amœboid tissue of the lymph-islands, or nodes; which, however, seldom produces tumours, for the simple reason that this multiplication by fission is its regular life-function, only the cells produced, instead of uniting to form a tissue, are scattered separately in the blood-current. Occasionally, however, even this simple correlation becomes disturbed, and we then have one of the most malignant and rapidly fatal of malignant growths—lympho-sarcoma. Rob a fat-cell of its adipose contents, and it becomes as nearly a typical mesamœboid cell as can be found in the body, a white blood-cell which has simply thrown out processes of attachment. Here, as everywhere else in nature, the almost axiomatic law holds good, that the more primitive a cell, the more easily it is capable of reproducing itself.

Moreover, from the very nature of its function and structure as a storage place for reserve food—materials for the rest of the body—there is no cell in the body which so frequently is called upon to sacrifice itself, so often placed, as it were, outside of the general body-scheme of vital nutrition, as the fat-cell. Not merely the fat proper, but the very cells which contain it, disappear completely in the course of starvation before any of the more vital tissues are drawn upon. Even the frequency of fatty tumours must be simply infinitesimal in comparison with that with which innumerable groups of fat-cells are completely eliminated and absorbed in the body-struggle, without any attempt, so to speak, at multiplication in self-defence. Fortunately, the fat-cell is the literal sheep of the body-politic, in disposition as well as function, with none of the aggressiveness of his more highly specialized brethren, the gland-cells; thus our most frequent tumour is at the same time our most innocent.

The fission impulse usually occurs only in a single group of cells, but it may of course simultaneously or successively affect a whole series of groups, and thus give rise to the extraordinary "diffuse" forms of fat tumour, which are so common about the neck and upper part of the chest and shoulders; or it may appear in a number of widely scattered centres and give rise to multiple lipomata all over the surface of the body. I have a case now under observation in a vigorous man of forty, under whose skin can be detected between twenty and thirty of these tumours, ranging from the size of a hazel-nut to a walnut, these are scattered all over the surface of the body and limbs. They first attracted his attention twenty years ago, rapidly attained their present size, and have made no further progress since. Neither age nor sex appears to have any relation to their occurrence, nor have we the slightest clue as to the conditions which determine their localization, except the vague one that they are most abundant, as already mentioned, in the two great storage regions, and least frequent upon the head and face, where the bones are dermal in their origin, and the adipose layer relatively thin. In short, they appear to be simply the easiest and commonest form of peaceful secession to which the cell republic is liable.

From a comparative point of view, however, a most singular condition confronts us; it is that not only do the tissues of other animals *not* share this tendency in the same degree, but that, on the contrary, fatty tumours of any description are extremely rare in animals, either wild or domesticated. In fact, almost the only instances reported seem to be a few cases of pedunculated subperitoneal lipomata occurring in the appendices epiploicæ of the colon in horses, oxen and sheep, collected by Sutton; a small number of fatty tumours in the mesentery, and under the peritoneal coat of the colon, reported by Friedberger, and two under the skin of the fore-leg in horses, by Macfadyean. The only cases I have seen personally were two in the last-mentioned situation. When we remember that nearly all our domestic animals, except the horse and the dog, have been bred and selected for centuries, with special reference to their power of producing excessive amounts of fat at an early age—"feeding kindly," as the farmers say;—then the rarity of fatty tumours in their case, appears to be all the more striking. The improved breeds of the pig, for instance, whose ancestors originally weighed from 100 to 150 pounds at five years of age, now reach from 300 pounds to 350 pounds at nine months, and two-thirds of this is lard. To all appearances, they are lipomata on legs.

The "beef breeds" of cattle have undergone a similar hypertrophy, from a weight of 750 pounds at four years to one of 2,000 at three; and the prize steer of a fat stock show is simply a huge roll of adipose tissue, with just bone enough to support it and with scarcely enough muscle to carry it about—as I once heard a Western farmer describe it, "the fat just sticks out all over him in chunks."

And yet in both these cases every ounce of fat remains in closest vital relations with the body whole, and will be promptly and systematically burnt up in starvation. Not a single "chunk" of that huge roll of subcutaneous fat is on record as having persisted as a lipoma!

But there are instances even more singular than this. For centuries the sheep of Kashmir and other Himalayan slopes, have been celebrated for the toothsomeness of their flesh in general, and of their fat tails in particular. These latter are so highly esteemed by Asiatic epicures, that they have been enormously developed by careful selection, until they have come to attain the dimensions and shape of a small bolster, and a weight of twenty to thirty pounds. So unwieldy are they that we are gravely assured by travellers that small wooden trucks or toy-wagons have to be placed under them, in order to permit the sheep to move about comfortably, and anyone who has seen a living specimen of this sheep can readily believe this, so huge and unwieldy is the overgrown member. A superb specimen is now in the London Gardens, but cannot be exhibited on account of the disfiguring effect of its monstrous tail, whose appearance, it is feared, would shock the delicate sense of propriety of the British public.

Here we have not merely an excessive deposit of fat, but also in an abnormal and isolated position; and yet it responds to the starvation test almost as promptly as the ordinary *panniculus adiposus.*

Not only so, but the tendency to fat formation here will not be transmitted unless it be of value to the organism. Repeated attempts have been made to breed these sheep upon the richer pastures of lower levels, with the invariable and disappointing result that the peculiarity, being no longer of service where there is no six months' winter's fast, falls in the internal struggle, and disappears or diminishes markedly in a few generations.

Now, to what is this extraordinary difference in tendency to tumour-formation due, in tissues so similar in every way as the fat-layers of man and of the other mammals?

Almost identical as they are in structure, there is, however, a well-marked difference between them in function. I cannot help thinking that this may have some bearing upon the problem, although I would only venture to suggest it as a possible explanation. It is that while the fatty layer in animals, even under domestication, plays an active part in the seasonal variations in the body-weight, in man it has practically ceased to do so. Of all our domestic animals which reach maturity, and which are used for breeding purposes, the storage tissues are actively exercised every year by a marked autumnal increase in the time of plenty, and by an equally marked winter and spring decrease.

If anyone doubt this statement, let him look at a herd of cows and heifers in the fall or the early winter, and again when the grass first comes in spring.

Except, of course, in the case of pedigreed stock, no farmer expects to bring his cows and "stock cattle" generally, his ewes or brood sows, through the winter and spring with a loss of less than 10 per cent. of their weight, indeed it will often reach even to 20 per cent. In the breeding-females, this seasonal variation is accompanied—or substituted—by the marked loss of fatty tissue during lactation, which of course, in most of them, occurs as a yearly phenomenon. These fluctuations, of course, do not occur to the same degree in sheep, cattle, or pigs fattened for the market; but, as these are seldom or never bred, and in many cases are either castrated or spayed, they exert no influence on the race.

The same variations necessarily occur in animals in a state of nature; so that I think it may be safely asserted that in all mammals, outside of our own family, frequent and more or less regular, active fluctuations of the fat-layer, constantly occur from seasonal or reproductive influences; in other words, their fat is still actively functional.

What is the case in our own species? Ever since the dawn of civilization, man's chief effort has been to render himself dietetically independent of the fluctuations of the season; and in this struggle civilized man has so markedly succeeded, that he has not only completely broken all connection between his periods of reproductive power and food-supply, and become unlike any other animal in the state of nature, capable of reproduction at any season of the year; but he has also almost annihilated the seasonal variations of his fat-layer. Such variations as do occur are usually the reverse of the natural ones, namely, an increase in the depth of winter and a decrease during the summer, due chiefly to variations in exercise and perspiration. His winter-fat is a mere surplus product, and instead of being of value as a reserve supply in the normal "famine-time" of late winter and early spring, becomes then a distinct incumbrance, which has to be got rid of by Lenten observances, "spring medicines," "spring-fever," the "agues of March," and profuse perspiration, before the body is in proper condition for the outdoor life of spring and summer. Fat in the animal is an absolute vital necessity, and is accordingly active; in man it acts chiefly as a lubricating and packing material, and is proportionally stagnant. In the latter, it gives rise to tumours; in the former it does not. The one period of human life, in which it unquestionably does display positive storage functions, is during childhood, where it seems to act as a reserve material for the exigencies of growth: and this is the only period in which lipoma is comparatively rare.

Next in order of frequency, among innocent tumours, come the group from what might be called the Connective Tissues Proper, namely, Fibroma, Chondroma and Osteoma. Of these, the precedence in frequency is usually given to Fibroma, but more careful methods of examination have reduced its preponderance from all sides. "Fibroma" of the uterus, for instance, is now known to consist of unstriped muscle-fibre; "fibroid" tumours of the breast are the thickened walls of adenomatous growths; "recurrent fibroma" is a spindle-celled sarcoma; "fibroma cavernosum" is an angeioma; and so it has gone on all sides, until Sutton now declares it to be one of the rarest of the benign tumours. And this is what might have been anticipated upon biologic grounds, inasmuch as fibrous tissue is a degeneration product of mesoblastic cells of low vitality and little powers of reproduction; indeed, according to Hertwig and other authorities, it may be questioned whether it be not an out-pouring from the neighbouring cells, and not a true cellular tissue at all. It is a frequent reaction—or degeneration—product, in the walls and tissues of other tumours, such as myoma, adenoma, or carcinoma (scirrhus). It obeys the usual morphologic law in being most frequent where its normal prototype is abundant, under the skin as *molluscum fibrosum* and "painful tubercle," and in the scars of wounds, where a rapid proliferation and subsequent atrophy of this tissue is taking place, as *keloid.*

Fibroid tumours are also rare in animals. They occasionally occur under the skin of the horse and in the walls of the nostrils, and also in the mammary gland of the bitch. These latter are, however, chiefly adeno-fibromata. In cartilaginous tumours we have, apparently, an interesting illustration of Cohnheim's theory, in that by far the largest number of them appear near the epiphyseal lines of the bones, where, as has been repeatedly demonstrated, "islands" of embryonic or infantile cartilage are quite liable to persist imbedded in the bone-tissue. And, as Virchow has shown, these islands are most common in rickety bones, and chondroma is peculiarly liable to occur in those who were rickety in early life. It may also occur upon the cartilages of the nose, larynx and joints, and thus follow the usual law of springing from like tissue. In animals, much the same regions are affected, but more rarely. Several cases have been reported in the testicle of the cat, and I have found a large specimen springing from the scapula of a sheep.

Tumours containing Cartilage, found in organs where this tissue is not normally present, as the parotid gland and the testicle, are now regarded as, usually, sarcomata, whose "embryonal" cells very easily undergo this change.

Much the same may be said of *Osteomata*, which are usually coated, or capped by cartilage, and are roughly defined by Sutton as "ossifying chondromata." They chiefly affect epiphyseal lines in the neighbourhood of tracts of cartilage in bones. When found where bone is not normally present, they are usually sarcomata. The division of exostoses has an even closer relation to normal ossifying processes, as these growths are peculiarly liable to occur in the tendinous attachments of muscles. Bony tumours are common in all classes of vertebrates, even in fishes and reptiles. In fact, from one to a dozen of them appear to be almost normal occurrences upon the fin-rays of the fish *Chætodon*. They are quite frequent upon the bones of horses, and in the frontal sinuses of oxen, weighing as much as sixteen pounds, according to Sutton; or, projecting into the cranial cavity, they have even been described in veterinary literature as "ossified brains." I have also found two small rounded tumours of this nature upon the wing-bones (*ulna* and *radius*) of a South American fly-catcher, and there are several specimens of these tumours in birds in the Hunterian collection.

A most interesting group are the *Odontomata* or tumours springing from some part of the embryonic dental sacs. A few of them spring from the enamel-organ, and hence really belong to the group of epithelial growths; but the vast majority spring from some part of the tooth-follicle, or from the dental-papilla, or from all these structures together. In every case they imitate accurately the layer from which they spring; if they proceed from the dental-follicle, they form fibrous cysts or masses containing teeth; if from the cement layer, huge masses of cementum, enclosing rudimentary teeth; if from the papilla, nodules of ivory-like dentine. All are common in animals, and the radicular or dentine-like growths are especially so in rodents, whose teeth grow from persistent pulps. They are believed to be due to misplaced or isolated buds or "islands" of embryonal tissues.

Of *myxoma*, *glioma*, and *neuroma*, it need only be said that each one springs from normal tissue of the type it imitates, and all are doubtful species, inasmuch as with the exception of nasal and aural polypi, most myxomata are really the result of mucoid (embryonic) degeneration in other tumours, lipomata, fibromata, and often sarcomata and cancers. *Glioma* is a diffuse overgrowth of the sustentacular fibrils of the brain-tissue and cord, and most of the tumours, to which the name is applied, are really sarcomata; while "*neuromata*" are really tumours of the fibrous tissue of the sheaths of the nerves (fibromata).

In *myoma* we have a condition of affairs most interesting for two reasons. One is that the neoplasm occurs almost exclusively in a region in which a power of enormous overgrowth on the part of the muscle-cells is a physiologic necessity, and the second that it is almost unknown in other mammals.

The first of these facts is a striking illustration of the contention that tumours are groups of the normal cells " run wild," usually following something of the normal lines of growth of the mother-tissue, as well as its structure. That these growth-tendencies are inherited and have a direct bearing upon tumour formation, is shown by the fact that almost the only place in the male body where these muscle tumours appear is in the *uterus masculinus,* or third lobe of the prostate, where they constitute a large share of that prostatic hypertrophy which is so distressingly frequent in men past middle life. As might have been expected where the new growth rudely imitates function as well as structure, these tumours still retain at times some relation to the body whole, as is shown by the fact that myomata of the uterus frequently shrink and disappear after removal of the ovaries and those of the prostate, after castration. They also follow the law of specially affecting "stagnant" tissues, as they are commonest in the female after thirty-five, and in the male after fifty; at which ages the reproductive powers are beginning to enter upon their decline. Smooth-muscle tumours are of course found in other organs, as in the wall of the alimentary canal, in the bladder and under the skin; but 95 per cent. of these tumours occur in either the uterus and its connections or in the prostate.

But how is it that they do not occur in the wombs of other mammals? In his enormous experience of some 12,000 autopsies upon mammals of every family, Sutton has only discovered one case, and that in one of our own order—a female baboon. In veterinary literature they are very seldom reported, and the few recorded are so scantily described that their real nature is far from certain. I have seen one specimen from the vagina of a bitch in Professor Macfadyean's collection, and they are occasionally found in the wall of the intestine of sheep and cattle.

There are only two conditions which, it seems to me, can be suggested as having any bearing upon this striking discrepancy. One is that, broadly speaking, reproductive power lasts almost as long as life does in the mammalia outside of our own species. Only when they are becoming positively decrepit through old age do mares, cows, ewes, sows, dogs, and cats cease to breed, and practically no wild mammals outlive either their teeth or their uteri. Certainly there is none of them in which anything corresponding to a menopause or stoppage of reproduction, just after the middle of the life-term, occurs. So that the "stagnant" or "superfluous" condition of the uterine tissues cannot occur to the same degree, a fact which I believe has a most potent bearing upon the tumours of this organ, both innocent and malignant.

The second difference is that ingeniously pointed out by Sutton, that the body of the human uterus is composed of two (Müllerian) tubes fused together, which remain separate as the "horns" of all other uteri. As it is precisely this region which is the site of myomata, the Fallopian tubes being almost exempt, Sutton thinks it extremely probable that the growths spring from embryonic remnants included during the fusion of the tubes to form the body.

The chief facts of interest about *Angeioma* and *Lymphangeioma* are that both, again, spring from the tissues whose name they bear, and whose type they reproduce; that the vast majority of them are congenital, and unquestionably belong in the Cohnheim group, and that they are both persistences and survivals of the embryonic vascular tissues with their abundant mesh of wide, irregular, and freely communicating blood and lymph channels. A nævus is simply an area of persistent embryonic skin, with its abundance of blood-vessels and pigment, as I ventured to suggest some years ago upon clinical grounds, and as Oscar Hertwig now affirms from an embryologic point of view.

One other mesoblastic tumour ought, perhaps, to be mentioned here, if only out of respect for its memory, and that is "*Rhabdomyoma*," or striated muscle-tumour, which is now generally regarded as a variety of spindle-celled sarcoma, whose cells have assumed a striated appearance.

The list of tumours which reproduce perfectly epithelial structures is a short one; in fact, there are only three names upon it, *Papilloma*, *Adenoma*, *Neuroma;* and the last of these is so doubtful that Sutton excludes it entirely, and Thoma, although declining to deny the possibility of newly formed nerve-cells in these tumours, considers it distinctly doubtful.*

Most *Neuromata* of the central nervous system are now regarded as malformations, or gliomata enclosing nerve-cells; those of the peripheral nerves are fibromata, and the same is true both of *tubercula dolorosa* and the "neuroma of the Paccionian bodies."

* "General Pathology," 1896, pp. 562-563.

This leaves us with but two classes, one numerous and simple, the other rare and complex. *Papillomata*, or warts, are simple overgrowths of the cutaneous or (rarely) of the alimentary epithelium. They differ chiefly in their physical characters, according to their situation, and the epithelium from which they spring. Thus, warts of the skin are usually dry, horny, and prominent; those of mucous membrane, soft, spongy, and villous. In all situations, as their name implies, they are simply hypertrophied papillæ. Of their cause we know nothing, except that, as they show a special fondness for the hands, face, and epithelium near mucous openings, and for the most "meddlesome" age, irritation seems likely to be a prominent factor. And this is borne out by their distribution in animals, where they are frequently found upon the penis of the horse and the bull, the mouth and foot-pad of the dog and other carnivora, and the lip of the lamb. Crops of warts are said to occur in the last-mentioned situation, soon after the animals have been turned out to graze in stubble-fields; they are supposed to be due to irritation by the sharp points of the stubble. I have seen one specimen in which the lips, cheeks, and palate of a dog were so densely packed with bleeding warts, which returned promptly after removal, that the animal had to be killed.

Cutaneous horns and *psammomata* of the pia of the brain and cord, complete this class. These latter are comparatively common in the cerebral ventricles of horses, where giving rise usually to no symptoms, they are not discovered till after death. I recently found two of these growths, of about the size of a small walnut and hazel-nut respectively, in the lateral ventricles of an old horse which had died of acute torsion-obstruction of the intestines, and had displayed no cerebral symptoms whatever. They do not give rise to the ordinary signs of brain-tumour, unless they exceed the size of a large walnut.

The last class of innocent epithelial tumours is a comparatively small one. Although *adenomata* are found in almost every glandular organ in the human body, especially in the mamma, the skin, and the ovary, yet, compared with the mesoblastic tumours and the much simpler papillomata, they are infrequent. They occur rather more frequently in animals, but their distribution is equally wide. They are fairly common around the anus of the horse and the dog, where they often reach a great size. They occur in the mamma of the bitch and the cat, where they are often mistaken for cancer, also in the liver of the sheep, and in the lungs of mice and rats. Wherever found, they imitate accurately the structure of the gland in which they appear, differing only in the fact that their cavity, or cavities, do not communicate with the duct of the parent gland. Hence they are very liable to undergo cystoid dilatation. In the mamma, so much fibrous tissue develops in their walls as to have earned for them the misleading name of "fibroma." By far their most frequent species is the "wen" of the sebaceous glands of the skin, although many of these are obviously simple "obstruction-tumours" from blocking of the hair-follicle into which the glands empty. They supply another illustration of the predisposing effect of "stagnation" in a tissue, as the sebaceous glands are purely appendages of the hair-follicles and have become superfluous over large areas of the body, by the atrophy or disappearance of the hair, whilst wens of the scalp are generally found in middle or later life, when the hair is beginning to fall. They are rare upon the hairy skins of animals; the only situations in which they have been reported, being the "velvet" of the antlers of the stag, and the margin of the anus in the dog.

To sum up in regard to "imitation" tumours, we think the following general conclusions are justifiable :—

(1) The simpler the tissue, the more frequently does it appear in tumours. The less-specialized tissues have retained more of the power of self-breeding. Fatty tumours are commonest, nerve- and striped-muscle tumours almost unknown, mesoblastic tumours are commoner than epithelial.

(2) The more actively functional a tissue or organ, the less liable is it to tumour-formation. Primary tumours of the lungs and heart are almost unknown; of the liver very rare; of the bones, sebaceous glands, and uterus quite frequent. Tumours and "stagnation" of tissues are closely associated.

(3) Regions in which embryonal inclusions are specially likely to occur, such as the human uterus, the jaws, the ovary and the epiphyseal line of bones, are correspondingly subject to the development of tumours.

CHAPTER X.

Reproduction Imperfect. "Parodies." Sarcoma. Carcinoma.

The second great class of tumours, springing from adult tissues, is distinguished from the first, by two striking characteristics, one Functional; the other Structural. Upon the *functional* feature; that of possessing the power of spreading through the body at the expense of other tissues, or dissemination, has been based their clinical classification as "malignant." Upon the *structural* one, of being imperfect imitations of the tissues from which they spring, "parodies," as I have ventured to term them, has been based their histologic classification. Nor is the co-existence of these two characters, which has been found so singularly constant in every species of both the mesoblastic and epiblastic divisions of the old clinical "cancer"-class, a mere coincidence.

What we term "malignancy" is one of the properties of immature tissue. The tissues of the embryo grow into, undermine, and absorb one another in precisely the same manner as the columns of cancer-cells do the surrounding tissues, the only difference being that the substitution process is sharply checked as soon as it has reached the limits demanded by the welfare of the body-whole. The hollowing-out of the medullary cavity, for instance, in the long bones, the absorption of the fangs of the milk-teeth, are carried out precisely in the same manner as that in which myeloid sarcoma will erode the shaft of the femur or the body of the jaw, and by giant-cells, which are in no way to be distinguished from those which have given its name to the malignant growth. Sarcoma travels along the veins and capillaries in precisely the same manner as that in which the vascular sheets of the middle germ-layer, thrust their way in between the folds of the peritoneum, through the choroidal fissure into the cavity of the optic vesicle, or in which the muscle-plates grow out into the interior of the primitive "limb-buds." The columns or "nests" of carcinoma burrow into the surrounding tissues in almost identical fashion with that in which the liver buds out into the ventral fold of the meso-gaster or the primary sebaceous follicles grow down into the subcutaneous tissues to form the mammary-gland. Nay, it is even believed by some observers, that in both these processes, the epithelial cells possess the power of turning their digestive secretions or ferments against the surrounding tissues, and literally eating their way through them. This is almost certainly the secret of the terrible "infiltrating" power of cancer.

We should, I think, expect upon comparative grounds, that the structural characters of immaturity, or primitiveness of type, would be associated with the functional characters of malignancy or infectiousness. The lower in the scale of life any cell or organism stands, the more rapidly and profusely does it reproduce itself. Fungi spread themselves over the surface of nutrient media as ice forms on a frosty night, whilst the rose blossoms but once a year, and two seasons must elapse ere the seed again produces bloom. The aphis runs through ten generations in a season, the butterfly barely one in a year. The fish produces ova by the thousand, the mammal by twos and threes. Similarly the lower in the vital and morphological scale are the cells of which a malignant tumour is composed, the more rapid is its growth, and the more pronounced its malignancy. The small-celled sarcoma and the "medullary" cancer, of embryonal cell-structure, are the most rapidly fatal of their respective classes.

This power of rapid breeding is not confined to the reproductive cells of the lower organisms, it extends to the tissues of every region of the body in the form of power to regenerate lost parts. Any part of a Begonia leaf will reproduce the entire plant. A worm may be cut into a dozen segments, any one of which will reproduce a head and a mouth, a tail and an anus, and ultimately an entire individual. The tissues at the junction of the lobster's claw with his body, or at the base of the star-fish's arm, will reproduce the entire member if it be torn off. Even in our vertebrate relatives, as high as the amphibia, toes, limbs, and eyes, may be replaced after their destruction. So that that abortive attempt to reproduce a secreting gland, which we call "cancer," is but a feeble reversion to much broader ancestral powers.

Not only is this true, but the more primitive the cell, the fewer are its vital necessities. The more lowly an organism, the more readily it will gain and maintain a foothold at the expense of higher forms or tissues, unless these latter be protected by alexins or sozins of some sort. Hence the deadliest foes of organized tissues are unicellular plant organisms, and the higher in the scale of being an organism rises, the less fitted it becomes to play the part of a parasite. Enormous fertility and few vital wants are the sinews and secret of parasitism.

The more complete the reversion to ancestral primitiveness and "savagery," the more dangerous the cancer or the sarcoma.

Nor does the parallelism between the primitiveness of the cancer-cell and that of other parasitic organisms end here. In the first place, this power of rapid reproduction is not only inherent in the lower forms, but it may also be assumed by the higher, under unfavourable conditions. This fact probably needs no illustration, as it is well known by gardeners that many cultivated plants "run to seed" in a poor soil so rapidly as to almost destroy their edibility. The further north maize is grown, the more rapidly it matures; so that Minnesota and Dakota corn is often systematically imported by Iowa, Illinois, and Nebraska farmers for seed-purposes. Both Darwin and Galton have commented upon the fact that in many forms of animal life, even including our own species, the more severe the struggle for existence, up to certain limits, the greater is the fertility.

Conversely, the more abundant the supply of nutriment to the individual, the lower its fertility. "Improved" breeds of cattle, sheep, poultry, and vegetables [that is, plants not grown for their seeds], are almost invariably slower or "shyer" breeders than the "scrub" or parental form.

Secondly, when higher forms, not usually parasitic, become so, they invariably revert to a less-specialized condition, and to that economy of vital necessities which goes with it. Very few vertebrates are able to revert sufficiently far back to become parasites. While this is true of the majority of the highest invertebrates, the insects, yet very many of these in their larval or embryonic form are actively parasitic, forming some of the most dangerous foes of higher organisms,—while all of those which have become permanently parasitic; whether partially, as in the case of that degenerate fly, the flea, or completely, as that degraded spider, the itch-mite, have suffered marked morphologic degradation, in proportion to the height of their power of tissue-invasion. Among the crustaceans the same rule holds good. The "fish-lice," and those innumerable forms which infest the alimentary tract of both fishes and their own higher relatives, are marked by the loss of their specialization as distinctively and invariably as by their powers of living at the expense of others. And even among worms the parasitic forms are as markedly inferior in height of organization as they are superior in infesting powers. Not infrequently, parasitic forms have been selected as the most primitive and probably most closely resembling the ancestral type of their group; they have even been placed in a lower class, whilst the traces of their descent from higher forms has been revealed, only after most careful study. And this is probably the true vital rank of the cancer-cell, which, as Hansemann well insists, in criticism of Cohnheim's theory, is not a cell of persistent embryonic characteristics, but an adult cell which has "lost its differentiation" ("*Differenirung verloren*").

The essence, then, of the "cancer-process" is a sudden reversion of certain cell-groups to an embryonic type, with a development of the powers of both rapid-breeding and "self-support" which pertain to this. *Whatever influences happen to condition this reversion, these are the causes of cancer.*

I say "causes" advisedly, for it is highly improbable and quite unreasonable to expect, that any single cause or class of causes can produce this reversion in such innumerable forms and in such widely-different tissues and situations. One characteristic, however, though brought about by various influences, will be found to be present in a large proportion of cases. It is that attitude of "*isolation*" from the body-whole, which we have found so frequent a forerunner of the benign tumours. This is especially the case with carcinoma.

The classification of malignant growths is in the nature of the case extremely difficult. Composed as they are of cells of embryonic type, they either in no way resemble the normal tissues from which they spring, or the resemblance is too remote and inconstant to be of any value for purposes of classification. Moreover, their cells, like all other primitive units, being extremely short-lived, are peculiarly subject to degenerative changes of all kinds, so that we may find two or three different forms of tissue, fatty, mucoid, fibrous, calcareous, in one small tumour.

This is peculiarly true of sarcoma, for in addition to the above possibilities, its cells have all the protean powers of the primitive mesoblast, to which they have reverted. Thus they may produce any one, two, or three of the tissues of this germ-layer, in the same tumour, no matter in what region or tissue it originates. These are, of course, but "fraudulent imitations," and their "success" only temporary, for sooner or later a further reversion comes, and the "chondro-sarcoma," or "myo-sarcoma," takes on actively malignant characters. Hence *adult tissue-terms applied to sarcomata must be regarded as purely descriptive*, and of little or no value for purposes of classification. This limits us, then, to terms referring to the shape and form of the cells, as a means of classification, and even these have to be used with caution and in a wide sense. Fortunately, however, they will also be found to correspond fairly accurately with the *degree of the reversion*, hence its functional characters and degrees of malignancy. With this understanding, as to its provisional and imperfect character, we shall make use of a division of sarcomata into four classes :—

1. Round-celled Sarcoma.
   Variations.—Osteo-, Chondro-, Fibro-, Lympho- } Sarcoma.
2. Spindle-celled Sarcoma.
   Variations.—Myo-, Fibro-, Chondro- } Sarcoma.
3. Alveolar Sarcoma.
4. Myeloid Sarcoma.

1. The first of these is not only the commonest form in the human species, but the most absolutely ubiquitous tumour known. It is found in all mammals, especially in the domesticated animals ; in birds, in snakes, in amphibia, and in fishes. Of seventy-eight tumours collected by Professor MacFadyean in thirteen years, among the domestic animals, thirteen were sarcomata, chiefly round-celled. Johne reports that of 128 tumours found post-mortem in the horse, sixty, or 47 per cent., were sarcomatous ; of ninety-three in the dog, 28 per cent., and of 104 in cattle, 37 per cent. were of this class.

Of seven tumours found in my necropsies at the London and Berlin Zoological Gardens, three were round-celled sarcomata, and two of these were in birds. Of five specimens secured at the *Thierarzenei Schule*, Berlin, through the kindness of Dr. Eberlein, two were sarcomata, one from the lip of a horse and one from the lip of a dog. This form of sarcoma is almost as innocent of structure as a bag of peas. It consists, in brief, of a mass of small round cells, with barely enough intercellular tissue to hold them together, most of its blood-vessels being mere chinks between the borders of the cells. As we should have expected from the extreme primitiveness of its elements, it is the most malignant tumour known.

It has also correspondingly wide powers of mimicry, and in various situations, will so closely imitate its mother-tissues as frequently to be mistaken for an osteoma, a chondroma, or a fibroma. Hence the terms which still encumber some classifications, "osteo-sarcoma," "chondro-sarcoma," etc., and the final revelation of the true nature of the growth is described in some text-books as a "sarcomatous change" in an innocent primary tumour. This imitation of the mother-tissue may be kept up for years, and yet an examination of the growth at any time would reveal a certain, in some cases, a large proportion of simple round cells, sufficient to reveal its true nature. Even though the primary tumour, on removal, may present all the naked-eye signs of pure osteoma or chondroma, yet it will often recur as an equally pure round-cell or spindle-cell sarcoma, and its metastases, when it suddenly becomes malignant, are almost sure to be of this character. Purely embryonic as these tumours are, still they have a distinct tendency to reproduce the mother-tissue, though with highly varying degrees of success, osteo-sarcomata are much more likely to begin in bone, chondro-sarcomata near the epiphyseal lines, myo-sarcoma in the uterus or under the skin, and so on. On the other hand, they inherit the architectural versatility of the original mesoblast to which they revert, and can equally readily build any form of connective tissue in any region of the body; the appearance of a tumour consisting of tissue, *e.g.*, cartilage, not normally present at the site, is now regarded as evidence, presumptive at least, of sarcoma.

The more complete, of course, the imitation of the osseous or other tissue from which it springs, then the less rapidly-growing and malignant will be the tumour. The only apparent exception to this rule is the "lymph" variety, but here we have a class of adult tissue simply imitated, which is probably the nearest living representative or survival of the primitive mesoderm of the embryo.

Like all sarcomata, it is extremely prone to mucoid degeneration, but as has been pointed out, mucoid tissue appears to play the same *rôle* in the embryonic, invertebrate, and lower vertebrate (oysters, fishes, amphibia), economy as fat does in the adult and higher vertebrate, so that mucoid degeneration in embryonic tissue is the equivalent of fatty degeneration in adult cells. The sarcoma cell is again displaying its primitive and ancestral character. And like other caseation processes, this one also leads to the formation of cavities or cysts.

2. The second great working-division of these tumours is known as the Spindle-celled. And while the distinction is a purely histologic one, and innumerable intermediate forms with cells between "round" and "spindle-shaped" are found, not to speak of "mixed" tumours, yet upon the whole this class appears to represent a slightly higher type of mesoblastic cell than the former. Its characteristic unit

is no longer absolutely unspecialized, but has taken a step toward the formation of the oval-celled connective and unstriped muscle tissue. And its functional characters correspond. It is distinctly less malignant, especially in the large-celled forms, less apt to infiltrate neighbouring tissues, less inclined to become mucoid or cystic, and more apt to successfully imitate a myoma, a chondroma, or a fibroma.

3. In Alveolar Sarcoma we appear to have to do with another slightly more specialized type of embryonic cells, tending to reproduce the vascular tissues. Hence a loose net-work of tissue, rudely resembling the spleen-pulp, whose cells are thrown into groups or alveoli by the branching and anastomosing of vascular trabeculæ. A step further and we have Angeio-sarcoma, or if the vessels be lymphatics, Lymphangeio-sarcoma.

As a considerable proportion of the cells of these tumours are of the primitive round shape, it has been urged by some authorities that they are really to be regarded as vascular-tissue variations of a round-celled sarcoma instead of a distinct class in any sense. Their separation, however, appears justifiable from the fact that the more specialized cell-elements determine the "function" of the tumour, its malignancy, for while osteo-sarcoma or chondro-sarcoma are as essentially and often as rapidly malignant as any other round-celled tumour, alveolar-sarcoma is upon a distinctly higher plane as to both stability and tendency to dissemination or recurrence.

4. The same is true in much more marked degree of the last division of Sarcomata, the Myeloid. These, as their name implies, are characterized by the occurrence of large multinuclear cells, which, however, are imbedded in a matrix of either round or spindle cells, and only form a comparatively small proportion of the tumour-mass. They determine

the character of the growth, however, to such a degree as to make it the slowest-growing, the smallest, the least likely to disseminate or recur of all the forms of sarcoma.

And the interesting thing about it is that it chiefly appears in those situations, viz., the central cavity of bones and the jaws, where cells strikingly similar to its own, the osteoclasts and odontoclasts, are normally present. The closest imitation of normal tissue coincides with the weakest malignancy.

Any one of these forms of sarcoma, except the last, originating in tissues normally containing pigment, *e.g.* the uveal coat of the eye or the *rete Malphigii* of the skin, may consist of pigment-bearing cells, and is then termed a melano-sarcoma. These are often ranged in a separate class, but inasmuch as their functions and characters are in no way affected by the pigment, but are determined solely by the type of the cells of which they are composed, the division is more confusing than helpful.

As a large proportion of them are round-celled, and, consequently, highly malignant, and as the secondary nodules are striking and easily recognized on account of their colour, Melano-sarcoma has often been given a much "blacker" reputation in the matter of malignancy than it really deserves. Those from the choroid take usually from three to five years to produce a fatal result, while the alveolar melano-sarcomata, which spring from the vascular tissue of moles and nævi, may grow slowly for years before commencing their rapid and fatal dissemination.

This form of tumour is tolerably common in the skin about the anus in both horses and dogs, and of the former species grey or white examples are most frequently affected. It grows slowly, seldom ulcerates, or gives rise to any trouble, except by its great size (30 lbs. to 50 lbs.), which may of itself necessitate its removal. It usually recurs after operation, and is often disseminated through the abdominal organs, on the other hand it may develop slowly for years without seriously affecting the animal's health. In both horses and men its gloomy and "satanic" colour has given it a worse reputation than it deserves.

These melano-sarcomata of the anal region of horses and dogs are curious structures in several respects. In the first place, like the carcinomata and melano-carcinomata found in this region in animals, they originate *not* in the mucous, tubular glands of the gut itself, but in a group of glands of cutaneous origin, which surround the anus (circumanal glands), and are probably scent-glands of sexual character. In the second place, not only are they most feebly and rarely malignant, but, unlike the loose and easily broken-down tissues of most sarcomata, are so firmly organized that wounds in them heal just as in normal tissues, and the open surfaces of their structure, left after an operation for partial removal, granulate and become again covered by epithelium with great rapidity.

Several of my veterinary friends assure me that they are sometimes obliged to leave large surfaces exposed after operative removal of these huge growths, and that these heal over by granulation as kindly as possible.

Finally, they are simply crammed with pigment, so much so as to "grit" under the knife on section, and display a literally coal-black hue. Often the amount of pigment is so great as to completely conceal the microscopic structure of the tumour, even in the thinnest section, before decolorization is resorted to. I have in my possession a metastatic node of this character, of about the size of a Tangerine orange, which is as firm as leather, and its cut surface as black as tar. It was taken from the lip of a horse.

One can hardly resist the impression that the excessive deposit of pigment is an almost causal factor in the slow proliferation of the growth. And it is a curious fact that the horses most prone to it, whites and greys, are those in whom large amounts of just such pigment have disappeared from the hair and skin. For, with the exception of Arabs and albinos, nearly all white and grey horses are born black or dark iron-grey, and do not "bleach" to their permanent colour till their fourth, sixth, or even eighth year.

I found a curious variant of the pigmented sarcoma upon the wing (forearm and elbow) of a dove dying in the London Gardens. The tumour affected the muscles and subcutanea, was of about the size of an acorn, and of a bright *saffron-yellow* colour, which is the tint of one of the principal dermal pigments in birds, zoonerythrin. Its structure was that of a round-celled sarcoma.

As to the influences which determine the appearance of sarcomata, whether predisposing or exciting, we are completely in the dark. They occur in almost every imaginable tissue and region of the body, and at any age from infancy to decrepit old age. There are, however, two peculiarities in their distribution which are worthy of comment. One is that in both man and animals, they distinctly avoid tissues or organs of high and constant vital activity, and especially affect tissues of sluggish vitality, whose function is almost purely mechanical.

Primary sarcoma of the heart, lungs, liver, or brain is practically unknown, and of the voluntary muscles and stomach extremely rare, while by far its commonest sites of attack are the skin-felt and fasciæ, the tendons, the fibrous coat of blood-vessels and the bones.

The same distribution is found in animals; for instance, Johne, in a collection of sixty sarcomata in horses, twenty-six in dogs, and thirty-six in cattle, found the bones the most frequent site of attack in all three species.

The other peculiarity is that by far its commonest age of attack is the period between twenty and forty, the stage in which the mesoblast of the body frame-work having reached its highest development, begins that slow decline which, when it arrives at the muscle-coat of the arterioles, we call old age. In other words, sarcoma would appear chiefly to attack tissues which are losing their vital activity, which are being practically "isolated," placed outside of the vital scheme, hence, as it were, they revert in self-defence to a primitive type capable of independent existence.

But this may be only a coincidence. Its contrast with carcinoma is three-fold.

First, its origin from the derived mesoblast, instead of the primary epithelium and the lesser power of burrowing and infiltrating which goes with this.

Second, the age-period of its attack, young adult-life instead of maturity and beginning old age.

Third, its lower organizing power. It imitates only a tissue instead of an organ. Often only a cell. Hence its complete absence of structure and even of stroma. But none of these throws any apparent light whatever on the question of its causation. Nor does its range of occurrence in the lower animals supply any data toward the solution of this problem. It has no more respect for age, organ, or species, than in the human family, although it appears to be distinctly more common among domesticated than among wild animals, and in dogs than in any other species.

From its simple structure and rapid growth the hypothesis of the infective origin of sarcoma has always proved an attractive one, and in favour of this we have its swift and easy dissemination, its tendency to follow venous channels, and its rapidly fatal toxæmic effects. Of late a number of instances have been reported of "sarcomata" in animals, which have proved capable of transference to other individuals of the species. Among the best known are the tumours of the genitals in dogs, which in structure and in their tendency to disseminate, resemble round-celled sarcoma. These are readily transmissible both by inoculation and through coitus. The careful study made of them by Bellingham and Smith has, however, shown that they much more closely resemble some form of infective granuloma, as they run a regular, self-limited course, usually ending in resolution and recovery.

For some reason the tissues of animals seem distinctly more inclined to the formation of defined, tumour-like growths, from infectious and other stimuli, than our own. The curious tumours in the livers of rabbits, due to coccidia, have often been mistaken for sarcoma, and even carcinoma. Many of the lesions of tuberculosis in animals are so firm, large and well defined, as to closely resemble sarcomata and fibromata. I have specimens of tubercular masses in the leg of a rabbit, the stomach of a spur-winged goose, and the pericardium of a sable antelope, which in texture, definiteness and bulk, would be taken at first sight for firm, round-celled sarcomata.

I also found a well-defined tumour of the pyloric region in a python, whose macroscopic appearance strongly suggested sarcoma, but which proved on microscopic examination to be an inflammatory growth, full of large oval organisms, apparently psorosperms.

On the other hand we have its histologic differences from any known granuloma, its absolute certainty to "breed true" in its metastases, every one of which is a copy of the primary tumour in point of structure, and its remarkable power of tissue-imitation. While from the clinical point of view there has never been established even a reasonable probability of the infective nature of sarcomata, inasmuch as we have few or no records of their spontaneous transmission from one individual to another. Out of hundreds of inoculation experiments which have been attempted, only a small percentage have been successful. It is highly probable that even these are not true "inoculations," but *transplantations*, which might have been carried out with similar fragments of any normal tissue. As for the parasite itself, while there have been scores of announcements of its discovery, all so far have failed of corroboration, and we are as far as ever from certainty as to its nature or even its existence.

Carcinoma.

In *carcinoma* we have to deal with a similarly immature or primitive type of cell, with equally disastrous and even more fatal properties. The process involved here is much commoner. Carcinoma possesses the power of invading and living at the expense of other tissues, of rapid multiplication, of sending out "spore-cells" to form colonies in other parts of the body, to even a higher degree than sarcoma. This indeed we should expect from its higher origin. Born of the dominant cells of either the ectoderm or entoderm (originally continuations of one and the same layer, Williams' "archi-blast"), which possess *ab initio* the power of dipping into and branching through the mesoderm of the body-mass in every direction, it is little wonder that its cells display, even in their degeneracy, such terrible though perverted hereditary powers. Descendants of the creators and hereditary monarchs of the body-state, they are the Caligulas of pathology.

Not only is their origin higher than that of sarcoma, but so is their plan of growth. However rapid or tumultuous the proliferation of their cells may be, they always show distinct traces of an attempt to imitate an organ, instead of a tissue, and that organ is invariably a gland. The celebrated "columns" of cancer are imperfect acini, packed with a mass of proliferating epithelial cells, usually grouped round a centre or a central cavity, and the "nests," which are even more characteristic, are simply transverse sections of these. Cancer "burrows" into underlying or surrounding tissues, in precisely the same manner that pouches of epithelium dip down into the submucosa to form simple follicles or peptic-glands, or into the subcutanea to form sebaceous or sweat-glands.

The essence of the process may be summed up in one word, *perverted gland-formation.*

Again, in order to attain all the fatal characteristics of malignancy, proliferation, infiltration, dissemination; the cell has merely to revert to its embryonic type and powers. And as Thoma specially points out, the more primitive the cell, the more malignant the cancer.

The classification of carcinomata is even more difficult than that of sarcomata, and for similar reasons. All their forms being imitations, of all shades of imperfectness, of one class of structure, it is hard to make any clear or constant distinctions between them. The division is most frequently made into flat-celled, round-celled, and cylindrical-celled, and these terms as describing the forms of epithelium from which the cancer starts are excellent, but as distinguishing characters of the later developments of its growth, they are often misleading. The round-celled is the most primitive of the three forms, with far less appearance of structure about it, and consequently the most rapidly fatal, on account of its terrific powers of growth and infiltration, whether it appear in the breast, the uterus, or the stomach.

The cylindrical-celled form is somewhat more specialized both as to the shape of its cells and prevalent regularity of the acini formed by them, at times so marked as to render some portions of it scarcely distinguishable from adenoma, under the microscope. Its functional characters correspond with this type, for it is slower in its growth, and is inferior in penetrating powers.

The cell of the "flat"-cancer (epithelioma) is, upon the whole, the most highly specialized of any, it is the farthest from the primitive type. Accordingly this class of tumours contains within its ranks the least malignant, the slowest growing, and most feebly penetrating forms of cancer, for instance, rodent ulcer.

However, any tumour of the last two classes may assume a round-celled type, and then become as malignant and rapidly fatal as any form in the first class; for instance, some epitheliomata of the lip or tongue, and certain tubular (cylindrical) cancers of the rectum and stomach.

In fact, as Thoma points out, those round-celled cancers which imperfectly reproduce the normal epithelium of the gland in which they originate are usually distinguished by a high degree of malignancy.*

Any of the cell-divisions of cancer, except epithelioma, may give rise to a series of widely different tumours, varying chiefly in regard to the amount and proportion of stroma and connective-tissue contained in them. At one end of the scale we have a mass composed almost entirely of rounded epithelial cells, held together and thrown into clumps by a

* "General Pathology," p. 601.

minimum of stroma, the *medullary* or *encephaloid* form; at the other a firm mass or felt of connective-tissue and blood-vessels, containing in its meshes, scattered alveoli of epithelial cells, the well-known *scirrhus*.

The difference between these depends upon the rapidity of growth, the degree of organizing power, and the power of penetration of the epithelial cells; in other words, upon their primitiveness. In the case of scirrhus, the epithelial buds penetrate so feebly, separate so widely, to allow space for the supporting-fibres and blood-supply of the gland they are imitating, they multiply so slowly, that the surrounding connective-tissue has abundance of time to set up a counter proliferation and surround them with a fibrous wall. Consequently scirrhus is the slowest in growth, slowest to affect the lymphatics, and the slowest of any form of carcinoma, except rodent ulcer, to break down. That the stroma in scirrhus does come chiefly from the surrounding connective-tissues is interestingly shown by the fact that in metastases to the shafts of bones, the stroma of the secondary tumours is composed in parts of osseous tissue.

In the medullary form, the cells multiply so rapidly, crowd upon each other with so little regard to any form of structure, and burrow so ruthlessly in every direction, that the surrounding mesoblast has no time to react, and scarcely enough stroma is formed to furnish the epithelial cells with an adequate blood-supply. Hence the rapidity with which these tumours either break down completely or, like other embryonic tissues, undergo mucoid degeneration.

Here again, the more embryonic the tumour the more rapid and fatal the malignancy. Indeed, Hansemann insists that the degree of departure, of course in a downward direction, from the normal type of the mother-epithelium, or *anaplasia*, as he terms it, is the measure of the malignancy of the cancer. Hence, he ranks *medullary carcinoma* as the most deadly form of malignant growth.

That the epithelium of carcinoma is simply exercising *against the organism* powers, which are possessed by and exercised for the organism by proliferating epithelium anywhere, is shown by the interesting researches of Leo Lœb * into the behaviour of the epithelium of the skin, in the healing of wounds. He found that in the guinea-pig the epithelium upon either side of a superficial wound fused itself into a syncytium or cell-mass, and began to bud out in branching processes, not merely across the wound but down into the clot which filled it, and into the injured tissues. These branches or arms bored through every form of connective-tissue, especially if injured, through blood-clot, or even through cartilage, apparently dissolving these by some ferment which they secreted, probably allied to trypsin. The familiar action of the epidermal tissues in cutting through and levelling off exuberant granulations is thus explained. Dr. Lœb also discovered a closely similar penetration-migration process taking place in certain areas of a cancer of the skin, and in a case of deciduoma malignum.

Is it any wonder then that in certain chronic ulcers, in the scars of extensive burns, in chronic fissures of the lips or tongue, certain of these epithelial buds may wander so far from their normal relations and function, as to take on independent existence, and by so doing give rise to cancer? It is probable, however, that this can only occur where other predisposing influences are also at work.

The suggestion that these branches dissolve the surrounding tissues by the secretion of an enzyme, is an extremely interesting one. It carries us back to most remote ancestral ages, for this is precisely the method by which the hyphæ of

* John Hopkins' "Bulletin," January, 1898.

the mycelium of fungi eat their way into the woody tissue of the tree-trunks which they attack. In these the secretion is closely allied to pepsin. The acid saliva upon the lingual ribbon of the whelk and other gastropods, which dissolves the shell of their prey, is a secretion of similar function.

Although it is impossible to demonstrate that cancer originates in grandular epithelium only, yet it seems to be highly probable, first from the striking similarities between cancer-structure and gland-structure; secondly from the direct connection demonstrable in many cases between a cancerous column or nest, and the acinus of a gland; and thirdly because of the almost complete absence of cancer from those epithelial surfaces upon which glands are not normally formed, viz.: the central canal of the nervous system and the pavement cells lining the alveoli of the lung.

Primary carcinomata of either of these quite extensive tracts of epithelium, is practically unknown, the few cases of either which have been recorded being extremely questionable. There is no other epithelial surface in the body of one-fifth of the area of either of these, of which the same can be said. The only form of malignant growth originating in the entire nervous system is *glioma*, which springs from the neuroglia, and as this is now known to be ectodermal in origin, it must be classed, upon embryologic grounds, with the carcinomata, though it shows no likeness whatever in its structure to carcinoma, but rather resembles sarcoma.

In its distribution, both in space and time, cancer has far more definite tendencies and more marked preferences than its sister "parody," sarcoma. While no age is absolutely immune from it, it is rare before the thirtieth year, and although no gland-forming tract of epithelium in the body, whether ectoderm or entoderm, is exempt, yet certain definite areas and organs are overwhelmingly liable to it. These may be given in the order of their liability as the breast, the uterus, the lips and tongue, the pylorus, and the rectum.

The influence of age as a factor has been recognized from the earliest times, and each additional series of cases reported, adds to its importance (especially since the real nature of round-celled sarcomata, many of which were formerly classified as "encephaloid cancer," has been recognized), until now the testimony is practically unanimous that it is the most constant and important single predisposing condition. For instance, in Paget's series of 622 cases, only 135 appeared before the thirtieth year, of Gross's 1,622, less than 20 per cent. appeared before forty years of age; the average age of 700 cases of uterine cancer reported by Hofmeir, was forty-five years; of 500 cases of breast-cancer by Roger Williams, forty-eight years; of 115 cases of epithelioma of the lips reported by Jonathan Hutchinson, fifty-eight years; by Jessett, fifty-one years. While Alberts* from an extensive collation of the records of the subject, concludes that beyond doubt there is a "predisposition" to cancer-formation, which increases with age, and Thoma asserts that this factor plays the principal part in the etiology of cancer. In fact, so overwhelming is the evidence, that it is scarcely needful to multiply statistical references, to prove that cancer is emphatically a disease of age, of declining vigour, of commencing senility.

But as Roger Williams† has well pointed out, it is not a disease of "completed" senility, for while unknown before twenty, rare before thirty-five, and reaching its maximum in both sexes between forty-five and fifty-five, it shows an almost equally rapid decline after this decade of age,

* Das Carcinom, 1887.

† "Diseases of the Breast," pp. 242-246.

becoming between seventy and seventy-five, as rare as between thirty and thirty-five, and after eighty as infrequent (relatively to those living) as before thirty-five. Thus, it is obvious that there is a certain disturbance of relation between the glands and the organism, during the twenty years (from forty to sixty years of age) following the attainment of highest life-vigour, or the first half of the period of decline, which peculiarly disposes the former, that is the glands, to the setting-up of cancerous processes. This period, we believe, can be shown to be that of the decay of the glands themselves, and those glands or organs which decay first, that is to say, the longest before the close of the life-period of the organism, the primary and secondary sexual characters, are overwhelmingly the most subject to the process. And what is significant in this connection, is that the ages both of the rise and the decline of liability to cancer, are almost exactly a decade later in men than in women.

So that it appears to be a question of senile changes and tendencies, but of the *glands rather than of the organism.*

In regard to the age-preferences of cancer practically all observers are agreed, but as to its regional tendencies there is wide divergence of opinion. Practically, no gland-bearing tract of epithelium, whether ectodermal or entodermal, in the body is exempt from it. When one attempts to decide which organ or region is most frequently affected by it, the more series of statistics one studies, the more doubtful the question becomes, for the organ most interesting to the particular observer or statistician seems to have a marvellous faculty of coming out at the head of the poll! For instance, German and other continental authorities (Virchow, Orth, La Salle, D'Espine) place the stomach at the head of the list (30 to 35 per cent.) in both sexes, while English and

American observers (Gross, Roger Williams, Bland Sutton, Bryant) give this position to the breast and uterus in females (60 to 75 per cent.), whilst they are divided as to whether the stomach (28 to 34 per cent.) or the mouth-parts (25 to 38 per cent.) rank highest in males.

One point however, emerges clearly from all these differences of result and opinion, it is that although the *organ* most frequently liable is apparently in doubt, a very small group of organs will be found, from all sources of information, to show a marked preponderance in this regard. The five highest names upon almost every list are practically the same, viz., breast, uterus, stomach, liver, and rectum in the female, and stomach, tongue and mouth, lip, liver, and rectum in males. A series of structures which, as we shall see, have but one thing in common, and that is marked ancestral instability. And even the apparent disagreement as to the relative rank within this group, resolves itself somewhat when we find that opinions and data group themselves into three classes. Those based upon or drawn from private practice or from records of all cases treated in a given hospital, in which the female genitalia, and the male mouth-parts, respectively, decidedly predominate. Those from mortality records, in which these organs are equalled or slightly excelled by the stomach and liver in both sexes; and, lastly, those from *post-mortem* records only, in which stomach and liver are distinctly most prominent. The explanation probably lies in the fact that the first class of findings most nearly represents the actual proportions of *all primary tumours*. In the second class, all curable or operable tumours (which, practically, are almost limited to the regions first ranked as most liable) have, of course, been excluded, and the patient's death is, in many cases, attributed to the organ whose involvement most directly caused it, whether this be the primary or secondary site of the process. This last condition is strongly suggested by the high rank accorded to the liver (second or third, with 13 to 18 per cent.) in these series, whereas *primary* cancer of this organ is comparatively rare.

While in the last series based upon *post-mortem* records it must be remembered that comparatively few cases of carcinoma of the breast, uterus, mouth-parts, or rectum, die in general hospitals, on account of the lingering nature of the disease, and the hopelessness of treatment in the later stages, and that there is so little to be learned by an autopsy in these cases, that it is very seldom carried out upon those dying outside of the hospital, and only as a matter of routine upon those within. The converse of all these statements being true of gastric, hepatic or intestinal cancer.

This then leaves two groups of organs far in advance in each sex, the breast and uterus in the female, and the mouth-parts (tongue, lips, cheek, jaw) in the male, with the stomach a fair second in both. In the female the preponderance is enormous. Thoma estimates that 70 per cent. of all cases of cancer begin in these organs.

The broadest and most reliable series of cases I have been able to find is that of Roger Williams,* who from an analysis of 7,297 cases of primary cancer consecutively under treatment in the medical and surgical wards of four large London hospitals (St. Bartholomew's, St. Thomas's, University College, Middlesex) finds that in the female the breast was the starting point in 40·3 per cent., and the uterus in 34 per cent., or 74·3 per cent. together. A much larger series by the same investigator, based upon the entire English mortality reports for the years 1868 to 1888, though liable to many more sources of error, attributes 34·7 per cent. to the uterus,

* Loc. cit., p. 234.

and 21·2 per cent. to the breast, or 55·9 per cent. to both together.

The cancer-mortality returns of Frankfort-on-Main * for the thirty years, 1860-89, assign 27·5 per cent. to the uterus, and 11·3 per cent. to the breast, 38·8 in all.

Taking Williams's series, for the reasons above given, as representing probably most nearly the actual state of affairs in primary cancer, we have no less than 74 per cent. of all cases of cancer in the female attributable to two closely allied portions of her reproductive organs. In fact, upon all the above tables, to these organs alone is due the much greater tendency of woman to cancerous disease, which according to the English mortality reports for the twenty-five years, 1848-72, including 177,300 cases of cancer, is 2·29 times that of man.

Are there any grounds upon which even a partial explanation of the extraordinary fatality of these two organs can be attempted? It can hardly be due to their sexual character alone, for the essential organ of sex, the ovary, like the testicle in the male, is seldom affected. Nor can it be on grounds of irritation or trauma, for the vulva and vagina suffer vastly more in this respect than the uterus, and the nipple and ampullæ than the acini of the breast, in which latter 90 per cent. of all mammary cancers originate (Gross, Delbet). Nor can it be the strain, fluctuations and accidents of child-bearing and lactation, for cancer of both of these regions is within 1 or 2 per cent. as frequent in the unmarried and the sterile as in the married and fertile.

There are, however, two striking biologic characters of these organs, one of which they share with the rest of the

* Cited by King and Newsholme, "Proceedings Royal Society," Vol. LIV., sec. 327, p. 239.

reproductive system, that they die long before the body does, and the other, which separates them from every other part of this system, that they have originated within comparatively recent times. In fact, they are individually short-lived, and ancestrally recent and unstable. Nor are these characters simply accidental or unimportant as possible factors in the setting-up of the tumour process. As we have already seen, among the innocent tumours, stagnation, isolation, or alienation of the cell-group concerned, is one of the most important predisposing conditions. And here we have to an extent unparalleled anywhere else in the body, not merely stagnation, but absolute extinction of function and atrophy of structure. In no other organs of the adult body have we a distinct, marked, absolute extinction of function, regardless of the general vigour, and long before the close of the life-term. Is it any wonder that the epithelial pouches of the mammary acini of the uterine glands, cut off from their food-supply, doomed to slow decay, thrust out of the cell-republic, as it were, should take to breeding upon their own account?

As Herbert Spencer has shown, the natural reproductive powers of the fixed cells of the body tissues are held in check by the influence of the entire organism, so that they never go beyond that precise point, which is of greatest utility to the latter. When, however, this control is relaxed or destroyed, the primitive powers of the cells assert themselves and hypertrophies or monsters develop. And it seems to me that in the case of the uterus and the mammary gland, at or just after the menopause, we have precisely this condition of weakened control. The gland has played its part, lived its life, henceforth it is no longer a working part of the living organism, and cancer is born. We have already seen, as both Roger Williams and

Mitchell* have pointed out, that it is precisely this isolated reproduction, this "discontinuous growth," as they aptly term it, which constitutes the very essence of the tumour process, and which is expressed by the term "autonomous" or its equivalent, in every accepted definition. Add to this autonomy embryonal characters on the part of the cells produced, and you have malignancy, the cancer complete. In view of the striking nature and high degree of the degenerative changes which regularly take place in these organs, the only wonder is, not that this "rebellion of the cells" takes place so often, but that it only occurs in from 3 per cent. to 5 per cent. of all cases.

The fact is, to my mind, most significant, that the only organs of the adult female body, which normally decay and die long before the rest of the body, become superfluous matter in the system, biological "dirt," in fact, are the starting-point of three-fourths of all carcinomata which occur in the entire body. *Functional isolation precedes pathologic autonomy.* Cancer has a distinct ancestral basis.

Not only is this true, but as Roger Williams† has also pointed out, the processes of cancer-formation in the breast are precisely the same in their earlier stages as those pushings-out of epithelial buds from the acini, by which the mammary gland is formed in embryonic life and enlarged at puberty, and again at every lactation. Indeed, Creighton‡ shows clearly that acini are found to be both during the preparation for lactation and the resumption of the resting stage, packed full of disorderly epithelium, scarcely to be distinguished from the early stage of cancerous alveoli. So long as the body has further use for these cells, in the

* "Philosophy of Tumour Disease," 1890.

† Loc. cit., p. 119.

‡ "Physiology and Pathology of the Breast," 1878.

future, these degeneration-processes are held rigidly in check, but whenever the final wasting, or "mustering-out" begins, this check is no longer present and cancer is possible.

The significance of the age-liability is great in this connection. It is the *precise decennium* (forty-five to fifty-five years) *in which these degenerative and purposeless changes are most active*, while the cells of the acini have still plenty of vitality, which is the period of highest cancer-liability. After the atrophy is complete, after all the "live" secreting-cells have broken down and been absorbed, the liability ceases almost as suddenly as it began. According to Williams*, cancer of the breast is as rare after sixty as before thirty-five. The transition-period is the period of danger.

The same is true of the uterus. The reason of the striking discrepancy in cancer-tendency between the male and the female genitalia is, of course, obvious. The function of the male organs lasts as long as life does, and such changes as occur in them take place *pari passu* with the general decay of the body. They are among the last organs to lose their possibility of function, instead of the first.

A curious fact, which may have some bearing upon the possibilities of the male organs in this regard, has been brought out by MacFadyean. This observer found that of twenty-five cases of cancer in the horse, collected by him, seven were in the penis, nearly double the number in any other organ, and *all of these in geldings*. Siedamgrotsky also reports the frequency of cancer of this organ in horses. Whether this liability has any connection with its extinction of function and consequent atrophy, is, of course, impossible to say. It is curious, to say the least, that the only animal upon which castration is systematically performed, and which

* Loc. cit., p. 244.

is permitted to live to old age, should be the only one to show a marked tendency to cancer in the male genitals.

The older writers used to allege the occurrence of cancer in the penis of the bull and the stallion, but these, on closer investigation, have been found to be warts of irritative or inflammatory origin.

This brings us to the question, if decay of function is the chief predisposing cause of cancer, why do not other parts of the generative system, the ovaries, and vulvo-vagina, suffer equally? There are three considerations which appear to bear upon this problem. One is that the normal range of atrophy is much greater in breast and uterus than in either ovary or vulvo-vagina. The adult "resting" uterus weighs 2 to 2½ ounces, the senile organ 5 to 6 drachms, a shrinkage of 60 per cent. to 80 per cent. The mature breast after the menopause shrinks to one-fourth of its bulk before seventy years of age. The reduction in weight of the adult ovary to the senile condition is barely 25 per cent., while that of the external genitalia is even less than this.

Secondly, the possibilities of emergency-growth possessed by these organs are even more strikingly superior. The normal uterus weighs 2 ounces, the uterus at term from 1 to 3 lbs., and the healthy breast increases its bulk from two to four times during a pregnancy.

The tumescence of the ovary during ovulation never exceeds 10 per cent., and the bulk of this is due to vascular engorgement, while all changes of the vulva and vagina are chiefly of this character. As in the case of myomata, a high possibility of normal "loyal" reproductive power is a powerful predisponent to the occurrence of autonomous, "rebellious" reproduction.

The last condition is an ancestral one, and, to my mind, of deeper significance than either of the others, and that is the phylogenetic recentness of both the organs. The ovary goes back to the hydra, the oviduct and genital aperture to the worm and the crustacean, but the uterus and the mamma are alike neomorphs of our mammalian family alone. As their name implies, none but mammals have a milk-gland; indeed, the development of the organ out of an ordinary sebaceous gland can be seen within the limits of this class itself, from the depressed "lacteal sinus" upon the abdominal integument of the monotreme, through the false nipple of the marsupial, to the true nipple and perfect gland of higher orders.

The same is true of the uterus, for although oviducts are present from the level of the crustacea, and distinct enlargements in their course occur in birds, reptiles, and even to some degree in insects, yet these are either double or unilateral, and the formation of a distinct sac or pouch by the union of both oviducts is practically confined to the mammalia. The elaborate egg-passage of the bird or the reptile is developed entirely from the left oviduct, the right and its ovary usually atrophying completely.

Indeed, the pear-shaped uterus with a single cavity formed by the complete fusion of both Müllerian tubes is so extremely recent a development that it is only reached in our own order, the Anthropoidea. Now, as Darwin has pointed out, organs which have recently been acquired or developed are apt to vary widely within the limits even of the species and to be in a condition of high instability. And, it seems to me more than a coincidence that those vital organs which are strikingly most recent, the lungs, the uterus, and the breasts should stand at the very head of the mortality and morbidity lists. From a biologic point of view, it seems only reasonable that the successful performance of certain vital functions for fifty millions of years should have endowed the stomach, for instance, with a stability and with powers of resistance vastly superior to those which the lung, with a third of that length of pedigree, and the uterus with scarcely a tenth, have had time to acquire. And if, as Roger Williams holds and goes far towards proving, a large proportion of patients with cancer of the breast, are the survivors of tuberculous families, it would almost appear that of certain, probably decadent, family groups, those who escape death by the decay of one of their most recent and unstable organs are distinctly liable to fall victims to disease of another at a later period in life.

And this view of the origin of cancer is, I believe, supported by such facts as we possess in regard to its zoological distribution. These are, however, few at best; in fact, the most striking thing about cancer is its rarity in the lower animals, whether wild or domesticated. Sutton, in his enormous experience of some twelve thousand autopsies upon birds, reptiles, and mammals dying at the London Zoological Gardens, has found only one glandular tumour, and that an adenoma in a phalanger. In my small series through the past winter I have found one glandular tumour of such curious atypical cell-structure as to render it doubtful whether it was an adenoma or a carcinoma. It affected the cervix uteri of a monkey.

A careful study of veterinary records and reports leads to the same conclusion, viz., that cancer is, compared with our own species, decidedly rare in the domesticated animals. Although the term "cancer" is used in a very loose and inaccurate sense in many veterinary periodicals, including bleeding warts, ulcerating adenomata, or fibromata, and all forms of sarcoma, many unquestionable cases of it have been reported in nearly all of our domesticated animals, especially the carnivora, as Rayer, Hansemann, Glass, and others, have pointed out.

The distribution of these is also singular. Instead of mammary and uterine cancer being the commonest of all forms, it is one of the rarest, and is found almost solely in the mammary glands of cats, and rarely of bitches and mice. A few cases of cancer of the vagina* in the mare, bitch, and cow have been reported by various observers, and I have seen one case in the vulva of a mare, and the tumour of suspicious microscopic structure, already referred to, in the cervix of a monkey, but the disease in these regions is extremely rare. (Mills, Müller, Flexner, Casper.) According to Wesley Mills, cancer of the stomach is fairly frequent in old dogs, but the commonest site of the disease in this species, is the anus, in this opinion Sutton and Glass also concur. Cases of epithelioma of the penis† and of the eyelid (Martin) in the horse have been reported.

Siedamgrotsky‡ finds both adenoma and carcinoma, starting from the anal glands, fairly common in old male dogs.

Müller reports a number of cases of carcinoma of the breast in old bitches, which is usually of the scirrhous variety (most of these are now known to be fibro-adenomata), and months and even years elapse before it attacks the lymphatics or begins to disseminate. He also mentions "cylindrical-celled" cancer of the uterus as of possible occurrence, but very rare. Rodent ulcers§ and epithelioma of the mouth, lips, and vagina also occur in aged dogs.

One of the largest, and the most admirably worked-out

* Highly improbable that these were examples of true carcinoma, because the existence of true glands, has not yet been demonstrated in the vagina of any mammal.—EDITOR.

† Patterson Illustrated Medical News, December, 1888.

‡ Cited by Georg Müller, "Diseases of the Dog," p. 237.

§ Georg Müller, "Diseases of the Dog" (trans. by Glass), p. 340.

and described series, which I have been able to find, is that of Professor MacFadyean, of the Royal Veterinary College, who, in thirteen years, succeeded in collecting sixty-three specimens of carcinoma and adeno-carcinoma. As this represents the result of a special use of Professor MacFadyean's extensive influence and acquaintance, his specimens coming to him from all over the English-speaking world; and of a standing announcement in his veterinary journal, asking for specimens of tumours, during the earlier half of this long period, it gives a fair idea of the infrequency of cancer in the domestic animals. Any one of our great London hospitals could have exceeded this number in half as many months.

In my visits to some of the leading veterinary colleges on both sides of the Atlantic, through the courtesy of the surgeons and pathologists, I have succeeded in collecting specimens of some twenty cases of carcinoma and sarcoma, but it is rarely that I have found, even in the best museum-collections, more than twelve or fifteen specimens of carcinoma.

All these, of course, are merely rough indications of the frequency of the disease in animals, indeed, in view of the comparatively small percentage of domestic animals, which die a natural death, and the small proportion of these that come under skilled observation, data for a direct and definite comparison are absolutely wanting, yet they are, I think, sufficient to justify the conclusion that cancer in animals is a rare disease, as compared with its frequency in our own species.

Casper* reports from the veterinary clinics of Berlin, Dresden and Munich, 1,131 tumours of all classes in 86,113 horses, 4,020 in 85,500 dogs, and 102 among 4,972 cattle, making "tumours" form 1·3 per cent. of all cases of disease

* "Deutsche Iierärztliche Wochenschrift," August 20, 1898.

in horses, 2 per cent. in cattle, and 4·7 per cent. in dogs. But, the term "tumour" is used in such a wide and vague sense in veterinary literature that these figures are of but doubtful value for the purposes of comparison with our own species, especially as no details as to the kinds of tumours or organs affected, are given in this report.

Johne's series of 325 tumours found *post mortem* in 4,439 animals, seem to have been much more carefully recorded and studied, and of these 47 per cent. in horses, 37 per cent. in cattle, and 28 per cent. in dogs were sarcomata, while 22 per cent. in horses, 8 per cent. in cattle, and 52 per cent. in dogs were carcinomata. Thus making sarcoma by far the commonest form of tumour in horses and cattle, and carcinoma the most frequent in dogs.

The distribution of these carcinomata in the various organs and regions is much more uniform than in our own species, for while strangely enough the kidney stands at the head of the list in both horses and cattle, with 32 per cent. and 50 per cent. respectively, and in the horse the antrum comes next, with 21 per cent., no other organ has more than 10 per cent., and very few more than 5 per cent. Nor does the distribution in animals, appear to show any distinct parallelism with that in man, for although the mammary gland in the horse comes third, yet the ovary and the testicle come next, instead of among the lowest, as in ourselves. In the forty-eight cases in the dog, the parallelism is still more completely lacking, for the thyroid gland stands at the head of the list with 35 per cent.; the liver coming next with 15 per cent.; the mamma about the middle with 8 per cent. and the uterus near the foot, with 4 per cent.

A list of fifty-one carcinomata in the dog, examined by Casper himself, comes a little nearer the human distribution, having the mamma at the head with 18 per cent., but here the likeness ends, for the liver and the thyroid follow next with 14 per cent. and 8 per cent., whilst the uterus and skin lie near the bottom, with 2 per cent. and 4 per cent. respectively.

The literature of cancer in veterinary publications is, however, small and very unsatisfactory. The importance and frequency of the condition may be fairly judged from the fact that some of the leading authorities on surgery and pathology devote only from one to three pages to the entire subject. For instance, the admirable "Comparative Pathology" of Friedberger and Fröhner, out of nearly 1,200 pages, devotes less than *four pages* to cancer in all its forms. The cumbrous and encyclopædic compilation of Lubarsch and Ostertag is even more disappointing than this, for while it devotes over 150 pages to cancer, 135 of these are given up to cancer *in the human species.*

And the actual cases are even fewer than the reports would indicate, for with a few honorable exceptions, veterinarian onkology is in much the same chaotic condition as our human science was in the days before Virchow. "Cancer" still includes sarcoma, and, indeed, any tumour which ulcerates or bleeds, and "tumour" equals "swelling." Even in the excellent "Surgery" of Möller—the veterinarian "Agnew,"—both actinomycosis and tubercle are gravely discussed under the head of tumours.

I have been unable to find a report of a case of cancer of any variety, or in any organ, in animals below the mammal.

In view of the fact that cancer is fully as fascinating a subject to the veterinarian as to the human pathologist, and has been made the subject of innumerable exploring expeditions on the part of the latter into the realms of comparative medicine, this rarity of cancer must be regarded as unquestionable, although doubtless many cases escape recognition.

Why should not the bovine or canine mammary gland or uterus, almost identical in structure and absolutely so in function, in emergency variations, in liability to injury or infection, show equal cancer-tendencies with the human? There is only one explanation which seems to me possible, and that is that these organs in animals seldom or never outlast their functions. In other words, *few animals outlive their uteri.* With them reproductive power lasts almost as long as life does, and that degree of "detachedness" of the genital glands, which is so constant in our own species, never occurs. Cows and mares will breed as long as they can walk and graze; indeed, many a mare is used for brood purposes chiefly after she is too old to work, and is killed as soon as this power fails, and sows and ewes cease bearing only when decrepit with age. Bitches continue to litter very late in life, indeed are seldom permitted to live out their full life-term, on account of the extreme unattractiveness of their appearance in their declining years.

Almost the only female domesticated animal which either naturally survives her reproductive powers, or is permitted to do so, is the cat; *and this is the only species in which mammary cancer at all commonly occurs.* It was reported at one time to be fairly common in old bitches, but MacFadyean, after examining a number of these growths, declares the great majority of them to be fibro-adenomata, though he reports three genuine cases, thus ranking it third in frequency in the dog. A few cases are reported in the udder of the mare, but not one as yet in the udder of the cow, the goat or sheep. So that the "hyper-function" and irritation theory of causation gets little support here. The greater liability of carnivora, than of herbivora, to cancer is to be explained upon similar grounds. To use a Hibernicism, the latter don't live long enough to die of it. The vast majority of the herbivora are killed for food, just as soon as they have attained their full growth or earlier, even those which are kept for breeding purposes are of course fattened-up and butchered as soon as they cease to be fertile.

The females of wild animals in a state of nature, cannot outlive their reproductive powers, any more than the males can their fighting powers, and in consequence are almost absolutely free from mammary and uterine cancer.

And, as these two organs are the starting-point of 75 per cent. of cancer in women, or of 50 per cent. of all malignant tumours in both sexes, if this theory be proved to have any validity, a large part of the immunity of animals is thus accounted for.

Another most important factor in their general immunity, is the comparative infrequency with which most domestic animals are permitted to live to old age. To reach the cancer period in fact. Just as with the uterus, so with cancer of the other organs, those animals which are not killed for food, develop a much larger number of cases than cattle, sheep and pigs. In MacFadyean's sixty-three cases, the dog and the horse head the list, the former with sixteen, and the latter with twenty-five, as against three in the cow, two in the ox, and one in the sheep. In view of the much smaller number of dogs which come under the veterinarian's observation than of horses, these figures would indicate a higher frequency in the former species. This is confirmed by the opinions of most veterinarians whom I have consulted. No case appears to have yet been found in the pig. MacFadyean states that nearly all his cases were in old animals, and Fröhner, in sixty-five cases in the dog, found only 10 per cent. of them under five years of age, and 62 per cent. between five and eight years. These two considerations, the absence of senility of the uterus and the mammæ, the infrequency of senility of the entire body, seem to be adequate to account for most of the relative immunity of animals from cancer.

I believe that the rarity of cancer among savage races, or even those of a low grade of civilization, points in the same direction. Travellers, medical and otherwise, are unanimous in their statements that cancer is conspicuously rare in savages in all parts of the world. Some of this, of course, may be due to our few and imperfect opportunities for observation, but it cannot all be thus accounted for.

Livingstone * says it is absent from large districts of South Africa, though fatty and fibroid tumours are common.

According to Jourdanet, it is almost unknown in the hot regions of Mexico.

Roger Williams, from an extensive study, finds it rare in all parts of Africa, and also in Brazil, Jamaica and Mauritius. While in thickly-populated countries like China and India it seems almost as common as in Europe.

Billing's report on the Tenth Census shows that the death-rate from cancer among negroes in the United States, is less than half that among whites, or 12·17 and 27·96 per 100,000 living, respectively. And this agrees with the unanimous testimony of our southern gynecologists, who all report that negro women are almost immune from uterine and mammary cancer, though unusually prone to uterine fibroids. Now, the longevity of savages (popular superstition to the contrary notwithstanding) is decidedly low, and the females are usually old women by thirty, or at most, forty years of age, and even by twenty-five in some races. They rapidly

* "Missionary Travels in South Africa," pp. 127 and 504.

become wrinkled and decrepit after the menopause, and there is but little opportunity for the occurrence of that fatal anachronism, a decaying uterus or mamma in a vigorous body, which I cannot help regarding as the principal factor in the production of cancer.

Sir William Kynsey, for many years chief medical adviser to the Government of Ceylon, a keen and careful observer, informs me that the native women there live to a considerable age, their powers of lactation persisting in a remarkable way, so that it is no uncommon thing to see an old woman suckling one of her grandchildren. And, most curiously, cancer of the breast is extremely rare among them, though other organs are not infrequently attacked. My friend, Dr. S. Tristram Pruen, who for several years was a missionary in Uganda, informs me that forty to forty-five is a "good old age" among the natives, who look as wrinkled and decrepit at that age as Europeans at seventy, and that cancer is decidedly rare among them.

It is not the decadence of the breast and the organism *together* which is a source of danger, but of the one before the other. The longer that life and vigour are maintained, after the cessation of the reproductive powers, the greater is the liability to cancer, in man and in animals alike. As both Roger Williams and Cripps have shown, the richer, the more prosperous and highly civilized a community, and the higher the class in that community, the greater is the cancer-mortality. The cancer-mortality of West London is double that of East London. And the higher any race or class stands in the scale, the more "well-preserved" are its women. The outlawed mammary acinus must have abundance of the "sinews of war" at hand to permit it to rebel successfully.

After the breast and the uterus, there are three other regions which occupy a prominent place in the localization-tables of cancer. These are the tongue and other mouth-parts, the stomach and the rectum. The first two divide the honours of highest rank between them in nearly all tables. And they are all regions of peculiar interest from a developmental point of view.

According to Williams's table of 7,297 cases of cancer, the mouth-parts play almost as prominent a rôle as starting-points of the disease in men, as the genitalia do in women, nearly 40 per cent. of all cases being attributed to them. It is possibly little more than a coincidence, but if we eliminate these two groups of organs in each sex, we reduce the cancer-liability to almost the same figure for both. Now, these regions, otherwise so dissimilar, resemble each other in two important respects, they both undergo marked atrophy during the lifetime of the individual, and they are both modified by the sexual function, one primarily and the other secondarily.

The first statement needs some little elaboration ; the loss of the teeth, and all the succeeding changes, the shrivelling of the gums, the wrinkling and falling-in of the lips and cheeks, the atrophy of the alveolar processes and of the angle of the jaw, all tend to place many areas of this region, richly supplied with glands both sebaceous and mucous, in that condition of detachedness, of isolation, which is so favourable to the inception of cancer. And, as we have seen, the age-liability of the mouth-parts to cancer, corresponds closely with the earlier and more active period of these senile changes, viz., the fifty-fifth to the sixtieth year. (Jessop, Bowlby, Hutchinson.) As in cancer of the breast, it is not the later period, after the atrophy has been safely accomplished, but the transition-period, in which the danger lies.

But the objection will be at once most properly raised, if this condition has any causal relation, why does it not also operate similarly in females, in whom, of course, similar changes occur? There is one difference between the sexes in this regard, which I cannot help regarding as of possible significance, though I offer it as a suggestion only, and that is that this region in the male is markedly modified by secondary sexual developments, while in the female it is not. The mouth-parts of the female are simply the persistent and enlarged structures of the child. The chin remains round, the angles of the jaw unobtrusive, the mouth-cavity and tongue small, the lips soft, round and full, the muscles of mastication unobservable, the vocal cords short, and the thyroid angle low and rounded.

In the male, on the contrary, the whole aspect of the region changes at, and after, puberty; the canine teeth project beyond the incisor level, the chin becomes square and deep, the angles of the jaw project, the muscles of mastication stand out beneath the skin, all their lines and areas of attachment becoming larger, rougher and more prominent. The male jaw is almost as readily distinguishable as the male pelvis. At the same time, the *pomum Adami* projects, the cords elongate, the resonance cavities of mouth and pharynx enlarge to match the heavier voice, the chin and lips become covered with the heavy beard, and the male facies is developed. After fifty years of age, recession of all these characters begins, until ultimately, in many cases, the voice, jaws and lips of the old man revert to the infantile type as completely as those of the old woman. The senile changes in the mouth-parts of the male after maturity, are no greater absolutely than those in the female, but relatively they are much more so. This, of course, may have no relation to the proneness of the male lips and tongue to cancer, but the coincidence, I think, is worth mentioning. It may also be noted in this connection, that the few cases which I have found recorded of cancer of the mouth-parts in the dog, have all, with one exception, been in old males, in the cases in which the sex was given.

MacFadyean reports a case of cancer of the tongue in an old male cat, and the lip in horses is occasionally affected by extension from the nose or antrum, but generally, this region is seldom affected in animals.

Another developmental fact of interest in connection with cancer of the lip is that it begins, in the majority of cases, at or near the "red-line" of division between skin and mucous membrane. In just that borderland region, part of whose glands, of identical structure and ancestry, are to produce sebum and hairs, while another part are to produce mucus. Indeed, as Culbertson * has recently shown, sebaceous glands may not infrequently be found upon the wrong side of the line, in the mucous membrane of our lips and cheeks, while of course many mammals develop hair in their buccal pouches. The "border" is proverbially unsettled and instable, whether in the body or out of it, and these regions of "epithelial transition" (lips, rectum, cervix uteri) have long been noted as cancer-belts. The red-line of the lips is a zone where neither mucus nor sebum is produced in perfection, many of the glands are of intermediate type, and we find the gland-bud in a state of "unbalance" which must strongly predispose it to independent growth. Your "borderer" is always the readiest to rebel. And it is, to my mind, a suggestive coincidence that 90 per cent. of labial cancers begin in this zone, and 95 per cent. of these in the region, as all the dermatological friends, whom I have consulted, inform me, with which my own limited experience agrees, where the hair of the beard first begins to turn grey, viz., along the margin of the lower lip.

* Proceedings, Association of American Anatomists, December, 1897.

Now, as to the two other especially favoured regions, the rectum and the pylorus. Of the first, it may be said, as of the mouth, that it also is a "transitional" tract. The two zones of greatest liability in the gut are precisely the line between skin and mucous membrane, and the inch above this; and, that between the ectodermal epithelium of the proctodœum (cloaca), and the endodermal epithelium of the hind-gut, at the juncture of its middle and lower thirds. Commencing senility is again a factor, the disease being commonest between fifty and sixty, and sex is a predisposing condition, as it is nearly twice as frequent in men as in women (Allingham, Williams). But there is no special wasting of this section of the gut, other than that which it shares with the remainder of the body, nor is this more marked in men than in women.

In dogs, we have the interesting fact that the process begins in, and chiefly affects not the rectal glands proper (Lieberkuhn), but a group of *circum-anal* glands which open at the margin of the anus and lie under the skin.* These are, probably, in the nature of scent-glands and are related to the sexual system, as in many other mammals. It is the tissues in this very region which are so frequently the starting point of melanotic sarcoma in white, gray, and sorrel horses. This appears to be the commonest site of cancer in the dog, as out of MacFadyean's sixteen cases in this species, five affected the anal glands.

Last of all, we come to that region which, disputing the precedence with either uterus or breast alone in the female, is, in Continental cancer-statistics, far at the head of male localities, namely, the stomach. In proneness to cancer, the mouth-parts run a close second to the stomach.

Indeed, the mortality reports for both England and Ireland

* Müller, "Diseases of the Dog" (Glass), p. 337.

(1868-1888 and 1887-1889), quoted by Williams, ascribe to the stomach 10·9 per cent. in females and 29·6 per cent. in males, and 22·4 per cent. in females and 34·3 per cent. in males respectively, placing it at the head of the list for males in both. The Frankfort returns for the thirty years, 1860-1889, list it at 18·3 per cent. in females and 29·2 per cent. in males, second and first respectively. This is a very remarkable preponderance of liability, especially in men, and second only to the female genitals in all lists, and the male mouth-parts in Williams's series of the London Hospitals. Obviously, there can be no suspicion, even here, of extinction of function and atrophy of structure, for if there is any organ which *must* of necessity live as long as the rest of the body, it is the stomach. Moreover, it is not only no "*parvenu*" but the hoary ancestor and creator of all the organs, and of the present body itself for that matter. We find, again, the age-liability, although here it is a little more elastic, varying from forty to sixty years. It is decidedly more common in men than in women, estimates of preponderance varying from 25 per cent. to 100 per cent. (Habershon).

The localization of the disease in the viscus is peculiar. According to Ziemssen and Osler, 60 per cent. to 70 per cent. of all cases begin in the pylorus, or pyloric region. Brinton says that 85 per cent. begin at, or near the orifices, while Wilks and Moxon state that the district to the right of a line drawn from the cardiac opening to a point four inches below the pylorus will include the starting-points of the vast majority of cancers. So that when we speak of carcinoma of the stomach we practically mean carcinoma of the pylorus and adjacent region. Now, when we examine this region, we find it to be the area of greatest structural variability in the entire organ. Along the greater curvature it is marked off from the main cavity of the viscus by a deep groove (sulcus pre-pyloricus), followed by a bulging, the *antrum pylori*, and frequently by a second indentation.

Above, along the lesser curvature, there is a similar indentation due also to the action of muscular bands, and over the whole region we find thickenings of the muscular coat in the form of curving and interlacing bands which vary greatly in different subjects. The mucous membrane of this region is thicker and more vascular, and is often readily distinguishable by the eye from that of the rest of the viscus. The pylorus itself also varies markedly as to thickness of muscular ring, projection of the mucous fold, the shape and the size of the opening. The opening is especially subject to stenoses of various kinds, from abnormal thickness of muscular bands, fibrotic changes, etc., as well as to a curious congenital hypertrophy of its muscular coat. The area is peculiarly liable to ulcers also, nearly 80 per cent. of all which affect the stomach, beginning within its borders, and, like cancer, they manifest a special fondness for the region of the lesser curvature. In fact, the region, as a whole, is anatomically variable and pathologically susceptible. And I myself believe that we have in this region, with its pouches, its folds, its half-effaced musculature, so far in excess of its present simple functions, the remains of the grinding-stomach or "gastric-mill" of our worm-like or crustacean ancestors, which has persisted in specialized form in the well-known gizzard of birds, as well as in certain edentate mammals, as in the great ant-eater and in some of the armadillos.

As to the liability to cancerous change of this organ in animals, it is placed second on the list—after the anus—by Wesley Mills and Glass, though MacFadyean only found it twice in sixteen cases, thus ranking it third in frequency.

In MacFadyean's twenty-five cases in the horse, it occurred three times, also ranking third. So that in the comparatively low frequency of cancer in the lower animals, the stomach may be said to rank as one of the principal sites of attack. The disease shows the same preference for the pyloric region, in all animals in which it occurs, as in our own species.

Of course, even if this be the case, it may have no connection whatever with the cancer-tendencies, but it is, to my mind, a striking coincidence at least, that the three regions in the alimentary canal which are notably ancestrally unstable and individually variable, the mouth and lips, the pylorus, and the rectum, should be so overwhelmingly liable to carcinomatous change as to be the starting-points of 90 per cent. of all cases of cancer of the entire food-tube.

With regard to the numerous other gland-bearing tracts of epithelium which may become the starting-point of cancer, it may simply be said that, while no special morphologic liability can be shown for most of them, *any* area, after the forty-fifth year, may become isolated, at any time, from both the rest of the organism and from its food-supply. That this, however, is much less likely to occur, where there is no special developmental reason, can be inferred at once from *à priori* considerations. This is confirmed by the fact that the regions already described, include from 70 per cent. to 80 per cent. of all cancers in the female, and from 50 per cent. to 60 per cent. of all in the male.

To sum up, I would beg to submit the following propositions, partly as outlining tentatively the evolutionary view of cancer-formation, but even more as a statement of problems requiring further investigation :—

1. Cancer may be defined as an attempt on the part of a gland to reproduce itself independently—a "gland-abortion."

2. The embryonal character of the cells of which it is composed, both causes and conditions its malignant properties.

3. It is most liable to occur in glands whose supply of nutrition is being cut off, while that of the rest of the body is maintained.

4. This condition is most fully met in the uterus and breast of our own species, hence its enormous frequency in man, and its extreme rarity in these organs in the lower animals.

5. Ancestral tendencies are of greater weight in the causation of cancer, than any of the influences which affect the individual.

CHAPTER XI.

Tuberculosis.—Types of Bacilli and Zoological Distribution.

The distribution of tuberculosis is world-wide. No climate, altitude, race, colour or condition, no species of bird or mammal is exempt.

It is more prevalent in temperate than in tropical climates, in cities than in the country, in herbivora than in carnivora, but nowhere is it entirely absent. At least, the wider our knowledge of the disease becomes, the more profound grows our scepticism as to allegations of complete immunity.

Thirty years ago it was widely stated and believed that certain altitudes and certain races were entirely exempt from phthisis, but, as Pflügge declared at the Berlin Conference, not one of these has stood the test of further investigation. Ten years ago we were assured that among our domestic animals, the horse, the goat and the dog are entirely immune, and the statement was extended to the carnivora in general and even to all wild animals. Now, however, we know by abundant evidence that, although much rarer than in bovines, tuberculosis is not a very uncommon disease in either the horse, the goat, or the dog, and that the two former are quite susceptible to it when inoculated. And although the flesh-eaters, both in animals and birds, have a high degree of resistance to tubercle, yet in captivity at least, numbers of them die of it.

As for our opinions with regard to the immunity of animals in a state of nature, we have, I fear, but little to base them upon, beyond our extensive ignorance both of their mode of death and of their condition at the time.

One may scour a country swarming with wild animals and birds for weeks and never find the dead body of one. The moment they fall, usually days before they would completely succumb, they are pounced upon by some keen-eyed scavenger, anxious for a meal. Post-mortems it is true are held upon nearly all of them, but of a kind of which no reports are published.

At all events, whatever immunity any of these may naturally possess, it rapidly vanishes in captivity, as the death-records of any zoological gardens, show with painful clearness.

According to some observers, its ravages are not even confined to birds and mammals, but may extend to the cold-blooded vertebrates. Bland Sutton has reported a case in a python, Blauvelt, one in a salamander, and Dubard and Combemale, a number of successful inoculations in fishes, turtles and frogs. In none of these instances, however, has the bacillus present been shown to be indentical with Koch's, nor does the process tend to disseminate widely from the site of the inoculations.

The term "tuberculosis" has now a single and perfectly definite meaning, the results of the invasion of the tissues by the bacillus of Koch. Although the term is primarily an anatomical one, yet in view of the fact that 90 per cent. of all "tubercles" found are due to the pressure of this bacillus, its application has come by universal agreement to be limited to the lesions of this germ. Indeed, the Pathological Society of London, after a prolonged and careful discussion of all the forms of anatomical "tubercle" and pseudo-tuberculosis, have unanimously recommended that in future the terms "tubercle" and "tuberculosis" be restricted absolutely to this one disease, and that the term "nodule" be applied to the anatomical lesions formerly known as "tubercles." So that the "tubercular" lesions of glanders, aspergillosis, and tuberculosis, for example, will be known as "glanderous nodules," "aspergillar nodules," and "tubercular nodules."

This would unquestionably be a great gain in point of clearness and precision, and would rid us at once of the irritating term "pseudo-tuberculosis," and the jumble of conditions which it is made to cover.

This term has been a source of great confusion in comparative pathology, on account of the large number of parasites, both bacterial and animal, which give rise to nodules, more or less closely resembling those of genuine tuberculosis. These although, with perhaps a single exception, differing widely in every other respect from the genuine disease, have been promptly dubbed "pseudo-tuberculosis," with appalling qualifying prefixes or suffixes. But now that we clearly understand that a morbid condition has no title whatever to the term "tuberculosis," simply because tubercles, in the anatomical sense, are present, we can get rid of all these confusing "pseudo" groups. Unlike their fewness in the human species, among birds and animals there are no less than four great groups of these nodule-forming processes, each with three to six different sub-varieties.

The groups are (1) *Bacillary*, (2) *Yeast* or Mycotic, (3) *Animal Parasitic*, including the "*wurm-knötchen*" of the Germans, (4) *Mould*, principally aspergillar. As these have already been partially described in the chapter upon Diseases of the Lungs, and will be further alluded to, I will merely say here that, although of such numerous varieties and sources of origin, with the exception of the bacillary and yeast varieties, they seldom produce serious systemic effects or lesions which really bear more than a superficial resemblance to those of true tuberculosis; and veterinary authorities are agreed, that all taken together, they occur scarcely more than one-tenth as frequently as true tuberculosis.

For some years this confusion of "pseudo" names was worse confounded by the differences which were found to exist between both the bacilli and the lesions of tuberculosis as it appeared in cattle and those found in bird-tuberculosis, both of which again differed from those of the human disease. So marked were these differences that even Koch himself was at one time in serious doubt as to the unity of the disease, but now it is generally recognised that the process is in all three classes a genuine tuberculosis, but due to a slightly different form of the bacillus in each. Whether these forms are entitled to rank as true species or only as varieties is still in doubt.

The point of practical interest is that these three diverging forms of the disease do not seem readily intercommunicable, indeed some of the respective forms of the bacillus are even non-inoculable, outside of their own species or class of hosts.

Straus, Gamalein, Wurtz, Nocard and a number of other observers have demonstrated that it is impossible to infect birds with either human or bovine bacilli, whether by subcutaneous or intra-venous injection or by administration in the food. Straus caused a number of unfortunate fowls to eat half their own weight of tuberculous human sputum mixed with their food without any injurious results.

Professor Theobald Smith, after a large number of experiments, comes to the conclusion that the human bacillus and its products are not virulent to bovines, that the two bacilli are distinct species, and gravely doubts whether bovine tuberculosis is readily communicable to human beings. And while, unfortunately, the direct experiment cannot be made, there is very little evidence to show the possibility of the communication of avian tuberculosis to our own species.

When the avian bacillus is successfully inoculated into mammals it "breeds twice" in a curiously definite manner. In birds, tuberculosis is almost exclusively abdominal in its distribution, the lungs being seldom affected and slightly even then, and both the guinea-pig and the horse when successfully inoculated with the avian germ—though highly refractory to it—develop an abdominal type of the disease.

In both of these animals successful inoculation with the human bacillus results in the development of the pulmonary type of the disease.

And since, as will be seen later in our discussion, each type of the disease, avian, bovine, human, has one or more anatomical lesions which are characteristic of it alone, and these are seldom found in either of the other families or classes, it would seem probable that the communication of one form of the disease to a member of another host-class is much rarer and more difficult than was at one time supposed.

INOCULABILITY OF FORMS OF TUBERCLE BACILLI.

HUMAN.		BOVINE.		AVIAN.	
Inoculable.	Non-inoculable.	Inoculable.	Non-inoculable.	Inoculable.	Non-inoculable.
Guinea-pig Rabbit Horse (?) Dog (?)	Bovines Birds	Guinea-pig Rabbit	Birds Man (?) Horse Dog	Rabbit	Guinea-pig Dog Man (?) Horse

And it must not be forgotten that some of Nature's most effective safeguards are completely evaded when the virus is injected directly into the tissues. The horse, for instance, is fairly susceptible to direct inoculation with human virus, but naturally almost absolutely immune, very rarely contracting the disease spontaneously, no matter what his exposure to infection from tuberculous grooms, drivers, etc., Even the guinea-pig, which is probably the most susceptible animal known, to direct inoculation with both human and bovine bacilli, seldom contracts the disease under natural conditions, and is quite difficult to infect through the stomach or respiratory passages. Guinea-pigs are bred and kept in hundreds, within the precincts of our research laboratories, and enquiries directed to several of my bacteriological friends, elicit the unanimous testimony that spontaneous outbreaks of the disease among them are almost unknown. Animals may be almost absolutely immune under natural conditions, and yet succumb when an overwhelming dose of the virus is injected into their tissues or blood-vessels.

There appears little doubt that the human, bovine, and avian types of bacilli are the descendants of one common form modified by their respective environments. And while it is yet debated whether their divergence has progressed far enough to constitute them true and distinct species, yet it does seem fairly certain that it has gone far enough to render it difficult for any one of them to thrive under the life-conditions of the others.

According to Leubard, Velars, and Combemale, there is yet another variety of the bacillus, the piscine or reptilian, differing slightly from the others in shape and culture characters, and capable of living in the tissues of cold-blooded animals. Leubard states that he discovered a nodular disease, in the foci of which these bacilli were present, in the bodies of a number of carp, living in a pond into which the sputa and dejecta of a consumptive patient had been thrown. That these proved capable of cultivation and infectious to other fishes and frogs. Also that human cultures injected into fishes, frogs, snakes, and turtles, assumed the piscine form. But his reports seem to lack confirmation.

Sutton has reported, in a python, naked-eye lesions closely resembling tuberculosis, and I have found in three or four pythons and other snakes, during the past winter, calcareous and fibrous nodules corresponding to his descriptions, one at least of which contained numerous bacilli not unlike Koch's. Sibley has succeeded in producing in snakes by human inoculation, nodular lesions containing bacilli, but without any generalized infection.

So that although it seems possible that the bacillus tuberculosis may find a temporary lodgment in the tissues of cold-blooded animals, we have no adequate evidence as yet, either of a generalized infection or of the existence of a piscine or reptilian type of the bacillus.

As to which one of the three recognized forms of the bacillus, is to be regarded as the ancestral or primitive type, we are entirely in the dark.

Indeed, it is possible that this honour belongs to something quite different from either of them, for an increasing school of bacteriologists, numbering such names as Metschnikoff, Hueppe, Fischel, Roux and Semuner, now declares that the tubercle germ is not a bacillus at all, but a parasitic stage in the development of a mould of the streptothrix order. Certain it is that under some conditions, the "bacillus" tends to develop into branched and sporulating forms, distinctly suggestive of a mould-mycelium, especially in the avian form.

If this be true then the three type forms are simply the descendants of this common mould, modified by their host environment. And as an illustration of the possibility of the total loss of its characteristic form on the part of a mould, I may mention that the apparently obvious mould-nodules, in the lungs of birds dying of mould invasion of the air-sacs at the Gardens, failed in no less than seven instances to contain any trace whatever of mycelium or any other recognizable form of mould-growth, even after the most careful and repeated examinations kindly made by Dr. A. G. Foulerton.

Whether among the numerous moulds which invade the air-sacs of birds, or even among the mould-flora of our cupboards and houses, will be found the parent form of the tubercle bacillus—according to Metschnikoff's theory—is a question for the future. Certain it is that dampness and the absence of sunlight, the two factors which mostly encourage mould-growth, are the most potent influences known in keeping up a high local death-rate from tuberculosis in all species, including our own.

Entirely dependent as tuberculosis is upon a *contagium vivum*, this is not the only factor necessary to its development. Infection is absolutely indispensable to the spread of the disease, but even the most abundant and prolonged exposure to this is not alone sufficient to produce it.

Widespread and fatal as it is, it is by no means indiscriminately so; in fact, it can be broadly said to follow certain lines in its spread with almost absolute uniformity. It is emphatically conditioned upon lowered resistance; present everywhere, it finds a foothold chiefly upon defenceless soil. It is one of Nature's most powerful agents for the elimination of the physically unfit, under civilized conditions, that is to say, where her primitive checks of "battle, murder, and sudden death," famine and pestilence, are measurably removed. Hence the striking degree to which it is found to be a disease of civilization, in the root sense of "citification." Scores of observations from every quarter of the globe prove this connection. The Bedaween of the Arabian peninsula, according to the French army surgeons, so long as they stick to their camels'-hair tents and wandering, open-air life, are almost free from it, but the moment they abandon this for village or town life in walled huts, it becomes quite common among them. The Khirgiz Tartars of the open steppes, suffer very slightly from it, but those tribes of them, which have become villagers and town dwellers, are frequently attacked by it. Among the wild or "blanket" Indians of our western plains, the disease is almost unknown, but upon the reservations, it becomes one of the chief causes of their rapid dying out, its death-rate among the Dakotahs, for instance, reaching nearly three times that among our white communities. The Indians of Peru, who live in the open country, are almost exempt, while their brethren who are huddled together in the larger villages and cities suffer most severely. And the same tendency holds good in even highly "citified" communities. The death-rate from tuberculosis in all of our larger cities rises from the "normal" average of 12–14 per cent. of the entire death-rate to 16–18 per cent. and even 20 per cent. And within the cities themselves, the more crowded the ward or district, the higher is the rate, so that its mortality rises in certain of the lower artisan quarters to nearly double the average rate (26 per cent.). Armies in barracks, and garrisons of forts suffer from it so severely, that though composed entirely of men in the prime of life who have comparatively recently passed a rigorous physical examination, its death-rate may almost equal that in the general community. Long-term convicts in prisons and the incurably insane in their asylums fall before it like sheep. From 30 to 65 per cent. of their high death-rate is due to it alone, and in some badly-managed institutions its fatality rises to the frightful pitch of 63 per 1,000 living, or more than three times the *total* average death-rate of the outside community.

Not even the odour of sanctity is any protection, for it attains even a higher "bad eminence" in the death-rate of cloisters than that of prisons, being responsible for from 60 to 80 per cent. of all deaths.

Precisely the same preponderance exists among the other mammals and among birds. "Pearl disease" *(Perl-sucht)* is practically unknown in wild cattle, range cattle, and herds in fenced pastures which have wide and free range and no "housing" in winter. It becomes frequent in cattle of limited range, amongst these from one to six per cent. are found to present tuberculous lesions after death, whilst it reaches a positively appalling prevalence in "barn cattle" generally and dairy cows in particular, notably in the Holstein-Frisians and other Dutch breeds. In the Hollandish breed, Nathusius states that nearly fifty per cent. are affected, and in certain districts of Pomerania, Schautz reports as high as sixty per cent. diseased. In both of these districts many of the cattle are not even pastured during the summer but kept in sheds and enclosures and fed upon grass, which is mowed for them daily. Indeed Brush has advanced the theory that human tuberculosis is exclusively a milk-born disease, existing only in those regions where cattle are confined for dairy purposes.

In pigs roaming at large or with acre pasturage, the disease is quite rare, in those kept in pens and styes quite common, although never at all as frequent as in cattle. The carnivora in the wild state appear almost exempt, and even our dogs and cats in their semi-confinement are comparatively so, but in the cages at the "Zoo" they become much more susceptible. Monkeys in their native forests are but little prone to it; while, in captivity, Shirley had great difficulty in procuring specimens which were free from it. Wild birds so far as our knowledge goes are immune, and birds of prey and insectivores comparatively so even in captivity; but our domesticated species and particularly fowls, are highly liable to attack.

The striking increase of this disease under civilization and confinement, appears to be due chiefly to three factors. First, an increased survival of the unfit, from the removal of natural checks furnishing a larger amount of susceptible material for its attack. Second, increased opportunities for the communication and spread of the disease. Third, a lowering of the vital tone and vigour of many individuals, due chiefly to over-confinement and insufficient exercise, air, and sunshine. Of these the third is to my mind the most important. The first is a factor which, I believe, must be reckoned with, for popular superstition to the contrary notwithstanding, savage races invariably have a *low* average longevity, a high death-rate, and an appalling infant mortality. Those who reach adult age must possess a considerable degree of vigour and toughness, or they would never have survived. For obviously, the child, who dies of enteritis or famine at three, will not swell the tubercular death-rate at three and twenty. Much of the supposed immunity of the "noble savage" from post-pubertal diseases is due simply to the fact that he does not live long enough to acquire them. The second factor, I am compelled to regard as of less importance than that usually attached to it, for the reason that the bacillus is so widely spread, that abundant opportunities of infection are afforded, even under the most favourable circumstances. We have all admitted the "t.b." within the gates of our body-fortress scores of times, nay more he has probably effected a lodgment in the tissues of two-thirds of us at some time in our lives, as will be shown later. As Clifford Allbutt remarked in opening the discussion upon tuberculosis at the Portsmouth meeting of the British Medical Association, "more than half of us have probably been tuberculous without ever knowing it."

Cases definitely proved to be due to increased possibilities of infection, or where even a reasonable probability of direct infection can be shown, are rare. Transmission even from husband to wife, or from patient to nurse seldom occurs. Indeed, the death-rate from tuberculosis among hospital nurses, is not so high as that in the cloisters, or among the nursing sisterhoods of the latter as in the purely devotional ones. Scarcely a single case of tubercle has developed among the nurses and internes of the Brompton Hospital for consumption in the forty years of its existence, and not one among those of Dr. Trudeau's Adirondack Sanitarium in its nine years.

The last factor I believe to be far the most potent, loss of vigour due to confinement. Infection is emphatically conditioned upon lowered resistance; the disease is a disease of weaklings. And this position appears to me to be decidedly confirmed by comparisons between people of the same race and stage of social development, whose birth-rate and dangers of infancy are practically the same, under different hygienic surroundings, and between animals of the same or allied families.

Nor is the extreme frequency of infection by tubercle merely an assumed one. The records of the *post-mortem* table support it in the most decided manner. Biggs reports that of a large series of cases dead of other diseases, distinct scars were found at the lung apices in 63 per cent. Buchner in some 5,000 cases found these apical scars present in 65 per cent. In a series of 125 successive autopsies at the New York Foundling Asylum one or more cervical, bronchial or mesenteric glands were found tubercular in *every* case. Out of thirty bronchial nodes removed from as many cases, taken at random, eight proved infectious to rabbits.

In cattle it is extremely common, though chiefly in "housed" cows, among which it may reach the appalling pitch of 50 to 60 per cent, vouched for by Friedenberger in Pomerania; 60 to 70 per cent. in Hildesheim according to Haarstick: while Bange in 53,000 cattle in Denmark (Royal Commission) found 38·5 per cent. affected. It is also very frequent among fowls and ducks, although I have not been able to find any figures reported. When we remember that the innumerable lesions of "struma" must now be classed under this head, that, as an eminent surgeon has recently declared, two-thirds of all the diseases of bone in children are tubercular, and that nearly all the meningeal and pleural inflammations of young life are of the same nature, we are justified I think in concluding that not only has each one of us run the gauntlet of exposure scores of times, but that nearly two-thirds of us have suffered a lodgment on the part of the bacilli at some time during our lives. Our diagnosis of tuberculosis is still made far too much by the result. If the patient survives "the symptoms," it was not tuberculosis, but "bronchitis," "apical catarrh," or of late years "la grippe."

As a contribution to the study of the influences which determine susceptibility to the infection, I wish to present a brief report of my observations in the *post-mortem* room of the London Zoological Gardens during the winter of 1898—1899.

The report is avowedly preliminary and incomplete, as my work upon the subject is still in progress, and it is obvious that any conclusions drawn from such a limited number of cases, can only be tentative or suggestive. But as the results obtained, agree singularly closely with those of veterinarian experience among the domestic animals, they are perhaps of sufficient interest to justify a brief statement of them here.

The three factors which seem of greatest possible importance in predisposing to infection are Race, Food, and Housing. I propose to note the influence of each of these, as illustrated in the results of my observations and the general death-records of the Gardens.

Taking up first the distribution of the disease among the different orders of mammals and birds; second, its incidence upon the carnivorous mammals and birds on the one hand and the herbivorous on the other; and finally the difference in its death-rate among animals and birds of the same orders kept in open cages or unwarmed sheds, and among those kept in heated houses during the greater part of the year.

One word as to the methods of diagnosis of the cases reported upon. The disease in animals dying in confinement is so well marked, and so characteristic, that not every case has been submitted to a bacteriological examination; type cases both characteristic and doubtful have been selected from time to time, and these have been kindly examined for bacilli by Dr. A. G. Foulerton and Mr. Geo. Newman, and the naked-eye diagnosis checked by the results. "Tubercles" are produced in other diseases, but most of them can be readily distinguished from the "genuine" form upon careful inspection, and comparative pathologists are agreed that at least 90 per cent. of all conditions, presenting well-marked "tubercles" in the organs, are produced by Koch's bacillus. As illustrating the possibility of separating the pseudo-tuberculoses, I may say that I have found in the present series, eleven cases of various forms of these, in addition to the forty-seven genuine cases, some of which were quite puzzling at first, but most of them clearly recognizable. The period covered by my report is from October 20th, 1898, to May 20th, 1899, with the exception of the month of March, making six months net.

In this time 213 autopsies were made and recorded, or about 60 per cent. of all the deaths occurring during the time, many of the animals, especially among the reptiles, being either unfit or unavailable for examination, or dead of obvious external causes which made their remains of no pathologic interest. Of these 213 autopsies recorded, six were upon animals dying by accident, and sixteen upon reptiles and fishes, which for the purposes of this paper are of no value, leaving 191 cases of death in birds and mammals. I may say however that a fourth variety of the tubercle bacillus, the reptilian has been announced by several observers, and that no less than four of the sixteen reptiles presented changes, which were suggestive of tuberculosis, two of which were found to contain bacilli, resembling the avian form in shape.

Out of these 191 deaths no less than forty-seven were caused by a well-marked form of tuberculosis, or 24·6 per cent., that is to say double the ordinary human rate.

Of the deaths 60 per cent. were in mammals and 40 per cent. in birds, while the proportion of tubercle was almost exactly the same in both. It would of course be absurd to attempt to accurately distribute the percentages of such a small number of deaths among all the different orders of mammals, so I have simply taken five great groups in each and worked out the distribution of the disease in these.

These groups have also been chosen with a view to giving a basis for the study of the effects of food upon susceptibility. The results can, I think, best be presented in tabular form :—

TABLE I.

	Total Deaths.	Deaths from Tuberculosis.	Per cent. of Tuberculosis.
MAMMALS—			
Primates	45	17	38 per cent.
Ungulates	9	3	33·3 ,,
Carnivora	21	1	4·8 ,,
Rodents	6	1	16·6 ,,
Marsupials	22	2	9·1 ,,
BIRDS—			
Raptores	12	2	16·6 ,,
Gallinaceæ	16	9	56·2 ,,
Parrots and Toucans	9	2	22·2 ,,
Water-fowl & Waders	27	5	18·5 ,,

TABLE II.

	No. Living.	Death-rate acc. to 6 mns.	Death rate acc. 5 yrs. avg.	Per cent. Death-rate due Tubercle.	Deaths by Tubercle per 100 living.
MAMMALS—		Per cent.	Per cent.	Per cent.	
Primates	155	58	60	37·0	22
Ungulates (Ruminants)	118	15	23	26·0	6
Carnivora	185	23	35	2·9	1
Rodents	75	16	85	3·9	3
Marsupials	58	76	45	15·5	7
BIRDS—					
Psittaci (Parrots, &c.)	300	6	14	7·1	1
Gallinaceæ	160	20	33	33·3	11
Raptores	108	24	54	11·1	6
Water-fowl	330	17	13	23·0	3
Struthiones (Ostriches, &c.)	19	32	35	28.5	10

(A) *Family or Race.*—It is I think fairly clear from the Tables I. and II. that race or family as such, or rank of development have but little direct connection with susceptibility to tuberculosis. In mammals the highest order, the primates, is by far the most liable per 100 living (Table II.), while next to it comes the lowest division, the marsupials. Ungulates and Carnivora which are usually ranked as on about the same level of specialization, are widely separated, the former having about six times the death-rate of the latter. Within the order of the Ungulates itself the most striking contrasts occur, the Perissodactyles (odd-toed) being almost completely exempt, even horses and asses under domestication, while the Artiodactyles (even-toed) are extremely liable. But there are marked differences even among the families of this last sub-order, the pigs being nearly immune, while the Ruminants are very susceptible, and of these latter the Cervidæ are almost exempt, not a single death from tubercle having occurred among the forty-one deer in the Gardens during the period covered by this report, while among the thirty-nine antelopes there were three.

Among the birds we find the same confusion of ranks, but in an entirely different order. The highest order listed, the Psittaci (Table II.) (the Passeres were omitted for reasons of convenience, but their death-rate is extremely low), have the lowest death-rate (1 per cent.); the lowest order was next to the highest (10 per cent.); the Gallinæ and Raptores, which may be compared in relative level with the Ungulates and Carnivora, the highest and third highest death-rates respectively, the difference between them being less than two to one, instead of six to one, in the analogous mammalian groups. The Anatinæ, which lie perhaps lowest of all the Carinatæ, have a low death-rate, in marked contrast with that of the higher Struthiones, their near neighbours in the list.

And while deductions from such a small number of deaths can only be regarded as tentative and indeed preliminary, yet the results correspond very closely with those of veterinarian observers for mammals and of Dr. Heinrot, the ornithopathologist of the Berlin Zoological Gardens, who informs me that tubercle is extremely common in grain-eating birds, especially doves, and very rare in flesh-eaters and song-birds.

(B) *Food and Food Habits.*—When we arrange our groups of mammals and birds according to their food-habits, we find what seems to be in the main a real correspondence with their relative death-rates, although there are some curious exceptions.

TABLE III.

		Death-rate by Tubercle per annum per 100 living.
MAMMALS.		
Vegetable Feeders—		
Primates		22
Ruminants		6
Marsupials		7
		Average 11·6
Mixed Feeders—		
Rodents		„ 3
Carnivora		„ 1
BIRDS.		
Vegetable Feeders—		
Gallinæ	11	„ 7·3
Struthiones	10	
Psittaci	1	
Mixed Feeders—		
Anatinæ		„ 3
Carnivora—		
Raptores		„ 6

In this grouping I have classed both the monkeys and the parrots as vegetable feeders, since although both of these receive a certain amount of chopped meat, milk, eggs, insects, etc., yet nine-tenths of their food is vegetable. Indeed, the keepers inform me that among the monkeys, only the American species (Platyrrhines), who form barely ten per cent. of the whole, receive animal food in any appreciable quantity.

These figures appear to point strongly toward a greatly increased susceptibility to the disease among vegetable feeders, and a much reduced liability among meat-eaters, both mammals and birds. And this corresponds closely with the results of veterinary experience, in which cattle, rabbits, and guinea-pigs are highly susceptible, pigs much less so, and dogs, cats, and rats almost immune; hawks, owls, and song-birds slightly susceptible, fowls and turkeys extremely so.

Here again there are, however, serious exceptions to the apparent rule: the horse, ass—indeed, all the odd-toed Ungulates—the goat and the sheep, all pure vegetable feeders, having marked resisting powers, and very seldom becoming infected. Evidently, although food-habits coincide more nearly with the distribution of tubercle than do racial divisions, yet there is some other additional factor involved.

(C) *Housing.*—The question of the influence of confinement in artifically-heated houses, or in unwarmed sheds, is an extremely difficult one to investigate, on account of the scarcity of fair parallels for purposes of comparison. For the most part only tropical and sub-tropical animals and birds are confined in heated houses, and only temperate or sub-Arctic ones in open sheds or uncovered buildings, and both of these classes would probably die much more rapidly than they do, were their quarters reversed. On the other hand it must also be remembered that in the scarcity of space in the Gardens, animals living practically out-of-doors may have, and often have, no more space for exercise or larger sleeping quarters than those in warmed houses, and that some of the older buildings and sheds are worse ventilated and lighted than the modern heated houses. So that even out-door animals may be as far from ideal conditions as in-door ones. Temperament and adaptabilities must also be taken into an account: an eagle in an open air forty-feet cage, for instance, is much more injuriously "confined" than a parrot in a four-feet one in a hot-house.

So that we find the results so conflicting as to preclude any positive conclusions. Among mammals we have both the highest (primates) and lowest (carnivora) tuberculosis rate in highly-heated houses.

Among birds the highest rate (gallinæ) is in the open air, the next in moderately warmed houses (struthiones), and the lowest, in the hottest house of all (psittaci). So that as between orders and families there is nothing to be deduced from this factor in their environment.

Between members of the same order, however, there are a few suggestive contrasts. Among the Ungulates, as already mentioned, during the past winter, not a single death from tubercle came under my observation among the forty-one Cervidæ and thirty-eight Bovidæ kept in open air houses and sheds, while three occurred among the thirty-nine antelopes in warmed houses.

The average life of the inmates of the monkey-house is about twenty months, while the Chinese (Tcheli) and Japanese monkeys in the outside cages at each end of the house have already survived thirteen and seven years respectively. They were, of course, picked and hardened specimens to begin with, but they certainly would not have lasted half that time inside the house.

Upon one occasion a female companion of a smaller species was placed with the older Tcheli and lived happily for nearly four years, when the pair took to quarrelling, so that she had to be returned to the house, where she died in six months. Another monkey presented to the Society, had lived out of doors in a garden in Islington for seven years, but only survived the monkey-house six months. The few facts available would seem to point decidedly in the direction of desirability of as little heat and as much fresh air as is reasonably consistent with survival. A conclusion which both the superintendent and assistant superintendent hold strongly, on the basis of a wide practical experience. And which is supported by the remarkable lowering of the death-rate following the addition of large out-door exercise cages, open even in winter in the continental and American zoological gardens. In Cincinnati the death-rate was reduced by this outdoor treatment nearly fifty per cent., and in Philadelphia has been lowered to fifteen per cent. per annum, barely one-fourth of the London rate.

It would appear that some influence connected with the food habits of both mammals and birds, exercises an effect more or less constant upon their susceptibility to tuberculosis.

Food habits may act in at least three different ways. *First*, by the food itself becoming the vehicle of infection. *Secondly*, by some direct nutritive effect of the food upon the organism, increasing or lowering the vigour. *Thirdly*, by the securing the food in a state of nature involving the attainment and maintenance of varying degrees of vigour and endurance.

The first of these possibilities has, I think, but little practical bearing, for while both classes of food are equally liable to chance infection, bacillus-laden dust, air, fluids, sputum, &c., meat of every sort has the additional possibility of being itself infected, and yet tubercle is nearly twelve times as common in herbivora as in carnivora.

For the second possible effect there is more to be said, as meat is unquestionably more stimulating, more easily digestible, and more nutritious in proportion to its weight than any form of vegetable food. Moreover, as the interesting experiments of Brouardel have shown, foxes and rats upon a carnivorous diet were almost completely refractory to infection by tubercle, while upon a vegetable diet, although they throve and gained weight, they became more than twice as susceptible. Calves, so long as they live exclusively upon milk, even from tuberculous cows, are almost completely exempt from tuberculosis, only from one in one thousand to one in five thousand having been found infected in the German slaughter-house inspections.

An interesting contrast in this respect, exists between the old-world monkeys and apes (Catarrhines) in the Zoological Gardens, and the new-world monkeys (Platyrrhines). As already mentioned the former are almost exclusively vegetarian, while the latter receive quite a fair proportion of animal food in the shape of eggs, meat-worms and either grubs or insects, and sparrows, which last they devour with great gusto. And if any of these last courageous little foragers venture into the house and large cages in search of scraps, they are pursued with astonishing agility, and often actually captured.

The reason why this element is included in their diet is that they simply cannot be got to live without it.

It may be nothing more than a coincidence, but of the thirty-five deaths occurring during the six months among the vegetarian Catarrhines, no less than seventeen were due to tuberculosis, while not one of the ten deaths among the Carnivorous Platyrrhines was due to this cause.

Upon enquiry of both the keeper and of the experienced attendant in the post-mortem room, I was assured that in their experience tuberculosis was quite rare among the new-world monkeys. As the death-rate from all causes among the new-world monkeys was slightly in excess of that among the old-world ones (sixty-two per cent. per annum as against fifty-eight per cent.), the discrepancy can hardly be due simply to the surroundings agreeing better with the former than the latter.

Various keepers of experience have assured me that it is only since the introduction of a considerable element of animal food into the diet of anthropoid apes that it has been possible to keep them alive in captivity for more than a short time. The seven years survival of the celebrated "Sally" at Regent's Park is regarded as largely due to her partiality for beef-tea, of which she partook largely, and which is now a regular article of diet with all the anthropoids.

In human tuberculosis, the most successful food-cure which has yet been found is to put the patient upon a diet consisting chiefly, and in some cases exclusively, of broiled beef-steak and hot water, and some form of highly nitrogenous diet is usually insisted upon in the open air sanatoria. In most of our American sanatoria this diet is strongly insisted upon, and my friend, Dr. Tristram Pruen, informs me that Walther compels his patients at Nordrach to take large quantities of milk and meat, especially in the form of ham and bacon, and that he finds this diet of the greatest value in his own sanatorium at Cheltenham. However, this can only explain a part of the divergencies, for several families of herbivora, for example the horse, the ass and the goat, have almost as complete an immunity as the carnivora.

In the *third* factor we find what seems to me by far the most important element in the relative immunity of flesh-eaters, and that is the resultant habits of life and the vigour and endurance entailed by them. That a carnivorous method of life in the majority of instances demands a higher degree of activity, speed and endurance, than a herbivorous one, needs, I think, little demonstration. And where, from any cause, this higher degree of vigour and dash has been acquired by herbivora, there immunity from tuberculosis follows. And as the degree of this vigour and activity is probably best roughly indicated by the size of the heart, relative to the body-weight, I have ventured to arrange my orders and groups again according to this character.

TABLE IV.

SUSCEPTIBILITY TO TUBERCLE ACCORDING TO RELATIVE HEART-WEIGHT.

	Per cent. of deaths by Tubercle.	Heart-weight : Body-weight.
MAMMALS—		
Primates	22	1 : 160
Ungulates (Ruminants)	6	1 : 220
Marsupials	7	1 : 280 (Opossum).
Carnivora	1	1 : 90
Equidæ	Very low.	1 : 100
Cervidæ	Very low.	1 : 100
BIRDS—		
Gallinæ	11	1 : 279 (Turkey).
Raptores	6	1 . 113 (Vulture).
Water-fowl	3	1 : 104 (Ibis).
Parrots	1	1 : 80

As will be seen, the variations in this regard seem to run more nearly parallel with the distribution of tuberculosis than any other yet suggested, but as I have only been able to find one series of measurements for birds (J. Jones in Smithsonian Journal, 1856), and a few scattered ones for mammals, and many of these are based on two or three, or even a single specimen, it can merely be regarded as an interesting and suggestive conclusion.

It however corresponds quite closely, but with the differences between birds and mammals, the former with their larger hearts, having an average death-rate by tubercle of 6 per cent. (per 100 living), as against a mammalian one of 9 per cent., and with the contrasts between the carnivora and birds of prey, with their large hearts, and the ruminants and gallinæ with their small ones. It also harmonises the curious differences between the horses and deer, and the cattle and antelopes, leaving however the sheep with its small heart and low tubercular death-rate a marked exception.

In our own species it has been suggested by more than one authority that the size and vigour of the heart was an important element in the predisposition to tuberculosis. Years ago Fothergill declared that the typical consumptive was small of heart and large of lung. The feebleness and rapidity of the pulse in even the earliest stages of phthisis are almost diagnostic. Dr. Pruen informs me that Bodington, the originator, over sixty years ago, of the superb open-air treatment of phthisis, considered the chief problem of the disease to be the weak heart; he devoted his attention more to strengthening the heart than to any other factor. Walther of Nordrach to-day holds almost identical views, regarding the state of the heart as chiefly responsible for the failure of the lungs to resist the bacillary invasion.

Altogether the conclusion to which this preliminary survey of the question of the distribution of tubercle points, is that it is a matter of vigour, endurance, and resisting power, rather than of race, food, or exposure to infection; and as these powers are usually higher in flesh-eaters than in vegetable feeders, they possess marked relative immunity.

CHAPTER XII.

Tuberculosis: Local Distribution of Lesions in Different Classes; Communicability and Methods of Spreading.

Having noted the varying degrees of susceptibility upon the part of the entire organism, in the different classes and orders of animals, it may be of interest to enquire what are the liabilities to attack upon the part of individual organs or regions of the body in the various groups, chiefly in the hope of getting some light upon the questions of the commonest channel of infection or port of entry for the bacillus, and whether certain organs of the body are points of least resistance in the organism, and tend to succumb in what Weissman terms "the internal struggle for existence."

Although the disease spares no family in order of mammals in confinement, and my brief series includes cases in kangaroos, antelopes, an armadillo, a jackal, a llama, rodents, lemurs, monkeys and apes, yet it cannot be said that its localization in any form presents any very striking differences from that in our own species. In all, the lung is the point of severest attack, and its lesions the usual cause of death. Tubercle in all mammals kills by the lung. As to whether this organ is the earliest to be affected, my *post-mortem* findings are not adequate to prove, as most animals which die of tuberculosis in captivity are simply crammed with it, and it is impossible to say with any safety which are the oldest lesions.

In the small number of cases in which a few tuberculous foci were found in animals dead by other causes, these were almost invariably in the abdomen, usually in either the mesenteric lymph nodes, the spleen, or the liver. In fact, the most striking thing about the lesions of tubercle in animals is their much more general distribution throughout the organs. Though in nearly all my cases in mammals the lung was most severely affected, yet in only 15 per cent. was it confined to this organ alone, foci being found in the spleen, liver, mesenteric nodes, and even kidney as well. In 18 per cent. it was confined entirely to the abdomen.

Veterinary writers are generally agreed that in the domestic animals—that is, in cattle, pigs, and rarely in horses and dogs—the lung suffers most frequently and most severely, and that here is probably the earliest site of serious invasion, but that in most cases foci are to be found in the abdominal organs also.

The curious exception to this rule of more widely-spread distribution in animals is the almost complete immunity of the bones and joints. I have only seen osseous tuberculosis four times in animals, once in the knee of a kangaroo, twice in the ribs of monkeys, where a tuberculous lung was adherent to them, and once in the jaw of a monkey. It does occur, but not with anything like the human frequency, it is regarded in veterinary literature as rather a rare form of the disease. Affections of the genito-urinary apparatus would also appear to be much less common in animals, although more frequent in the domesticated than in wild mammals.

A marked characteristic of the disease in the Bovidæ, whether cattle, antelopes, sheep, or gazelles, is its preference for the serous membranes, especially the pericardium and pleura. Here it forms the well-known grape-like or shot-like masses of dense fibrous tissue, sometimes containing thick pus in their interior, which studding the whole surface of the membrane, have given its popular English and German names to the disease, "the grapes," and "*Perlsucht.*" Both this special preference and form of lesion appear to be confined to this family, although the pericardium is certainly much more frequently affected in the other groups than in our own species. In two cases in monkeys I have found small nodules upon the surface of the heart itself, just under the pericardium.

Many of the lesions in other situations in bovines, appear to have this tendency to surround themselves with a dense fibrous envelope. Suppurating foci in the liver and lung will be found enclosed by a wall of fibrous tissue nearly a quarter of an inch thick. In a sable antelope the whole external layer of the pericardium was changed into a firm dense wall of new growth three-quarters of an inch thick, which retained its shape after the heart had been removed from its cavity, as if it had been a plaster cast. Tuberculous peritonitis, on the contrary, appears to be no more common in animals than in man, as I have found only three cases, all in monkeys. Tuberculous ulceration of the intestine is not uncommon, especially in the cæcum and colon of monkeys.

It may be broadly stated that purulent degeneration of tuberculous masses is much more rare in animals than in man. With the exception of the thick-walled abscesses in bovines, most foci in mammals are firm, well defined, caseous, and even fibroid masses, which often closely resemble true tumours. Even in the tremendous infiltration occurring in the lungs of monkeys, in which two-thirds of the organ is turned into a caseous mass, a cavity or even fluid pus is a decided exception. The mesenteric nodes, which may reach the size of a greengage plum, in monkeys, are usually firm, cheesy, or fibroid masses, and I have never yet seen pus in either liver or spleen, except in domesticated bovines.

The distribution of tuberculous lesions in birds is strikingly different. Instead of the lungs being the commonest site of attack, they are one of the rarest among the great viscera, and, in place of their lesions being the cause of death, I have only seen one case in thirty-five where they seemed to be so. The chief seat of the disease is in the abdominal viscera; first and most severely in the liver, next in the spleen, and third in the wall of the intestine and mesenteric nodes.

In only twenty per cent. of my cases were the lungs affected at all, and usually all that is to be found in them is one or two small, round, very firm nodes, which shell out of the lung-parenchyma in removing the organs from the chest. These are often of a brownish colour, and of about the consistency of very hard old soap; indeed, some of them are so difficult to cut as to suggest a keratinous or horny change in their substance. All tuberculous nodes in birds are firm and usually well-defined, and in many cases contain so much calcareous deposit as to render section of them with the microtome almost impossible.

Dr. Heinrot, avian pathologist in the Berlin Zoologischer Garten, informed me last summer, that they also often contained deposits of urates; these, however, I have not been able to detect in any of my cases as yet. I am, however, strongly inclined to agree with him that these hard, chalky, tuberculous nodules in birds, occurring in the neighbourhood of the joints, have been mistaken for gout, which latter disease is much rarer in birds than is usually supposed and reported.

My own brief experience, like Sibley's, does not agree exactly with Sutton's statement of some fifteen years ago, that tuberculosis in birds invariably began in the intestines or their lymph nodes, as both of us have found a number of well-marked cases in which no lesions in the intestines could be found.

The cause of death in tuberculous birds appears to be most commonly diarrhœa; but I should be inclined to regard this as more due to the condition of the liver and its secretions than to ulcerations of the intestines, which though occasionally present, are not common, and never in my experience extensive or severe enough to account for the diarrhœa and the fatal result.

The chief attack of avian tuberculosis falls upon the liver. In only 2 cases in 35 have I found it unaffected, while in about 20 per cent. it was the only organ attacked, and usually a glance at its upper surface is sufficient to base a diagnosis upon. It becomes enormously enlarged, fatty, and crowded full of hard, yellow nodules, from the size of a pinhead to that of a hazel-nut. The spleen comes second both in frequency and severity of attack, although in some cases it is even more severely damaged, being swollen into such a huge, caseous mass as to be almost unrecognisable.

Tuberculosis of the bones and joints seems to be decidedly more common in birds than in mammals, as I have found it in about ten per cent. of my cases, most strikingly in the knees of a peacock, the elbow of a stork, and the palate of a secretary vulture.

Pus is practically unknown in birds, not merely in tuberculosis, but also, in both my experience and that of Dr. Heinrot, under any circumstances. This may possibly be connected with the dryness of their flesh, their solid urine, and the remarkable extent to which all their tissues are permeated by pure air. I have found the heart-surface twice attacked, once in a curassow and once in a buzzard.

As to the distribution of tuberculosis in reptiles, I am afraid we must wait until the interesting question has been decided whether the disease actually occurs among them. Sutton was of the opinion that it did rarely, and Sibley some years ago succeeded in producing apparently tuberculous lesions in snakes by injecting cultures into their tissues. I have found lesions closely resembling both their descriptions in two pythons, two smaller snakes, and one tortoise. In the snakes these were firm, cheesy, and calcareous nodes, about the size of a small hazel-nut, under the skin of the neck region and in the intestinal wall and mesentery; while the greater part of one lung in the tortoise was packed full of a soft, flocculent, caseous material.

Dr. A. G. Foulerton and Dr. George Newman, to both of whom I am greatly indebted for valuable advice and co-operation in my investigations, kindly examined several of these for me bacteriologically, but with negative results, except in the lung of the tortoise, which was crowded full of suspicious-looking bacilli, which, however, did not respond completely to Koch's tests.

Do the facts of distribution throw any light upon the problem of the channel of infection? Only, I fear, the questionable illumination of casting a shadow of doubt upon our existing theories.

If the tremendous susceptibility of the lungs in mammals is to be accounted for by their being the port of entry for aërial infection, how are we to explain the almost equally striking immunity of the bird's lung?—to say nothing of the well-known experimental fact that if a guinea-pig or rabbit be inoculated in the flank or abdomen he usually dies of pulmonary tuberculosis, and this, too, in spite of the fact that the guinea-pig is extremely hard to infect through the air-passages, even by coating his cage-bottom or mixing his food with dried sputum, whilst fanciers assure me that under ordinary circumstances he is almost exempt from tuberculosis.

The air-passages of the bird are certainly no better protected against dust-contagion than those of the mammal, indeed, if anything rather less so, as the turbinate filter is less complete and the throat and trachea much wider.

Then if it is simply a question of exposure to aërial infection, it seems hard to understand why the lodgment should occur at the highest and most inaccessible parts of the lungs, the apices in our own species, and the dorsal borders on each side of the vertebral column in bovines, as Friedberger and Fröhner, Law and Stalker unite in stating that it does, only towards the posterior (caudal) border or base instead of the apex.

What seems to me a suggestive parallel is to be found in the localisation of glanders-lesions in the horse. Most veterinarians regard the glanders infection as entering by the alimentary canal, in the drinking-water or food, and yet its severest and most fatal lesions are as a rule found in the lungs. Most suggestive is the fact that if a horse be tested by the subcutaneous injection of mallein, and killed forty-eight hours later, his lungs will be found dotted with small, firm shot-like "tubercles," when no other trace of the results of the injection can be found. Even the toxin of glanders has a special affinity for the vertebral borders of the lungs. Schutz's interesting experiments have shown that when an excessive amount of infectious material is introduced into the stomach, although the lung is the most seriously affected of all the organs, the abdominal viscera are also attacked.

And this appears to me the most probable relation of the mammalian lung to tuberculosis. By whatever channel the bacilli are introduced, they find their most favourable soil for growth in the lungs.

Nearly all the veterinarians I have consulted are inclined to the opinion that the commonest channel of infection is through the alimentary canal, and my own limited experience seems to point in the same direction. It is probable that the distinctly greater frequency of abdominal lesions in the lower mammals than in man, may be due to the more voracious and less cleanly food-habits of the former, the larger amounts of infectious material swallowed, overcoming the resistance of the abdominal viscera as well as of the lungs.

That the organs of the body differ as to the power of their resistance to various infections, however introduced, can hardly be questioned. And the degree of relative resistance appears to vary in different species. Professor MacFadyean informs me that if a series of rabbits and a series of guinea-pigs be inoculated in the same part of the flank, from the same culture, in the former the kidney will be affected and the spleen exempt; in the latter the spleen will be attacked and the kidney will escape.

The morbidity of the mammalian lung in tuberculosis is, as we have seen, in keeping with its great susceptibility in other diseases. In any bills of human mortality, the three highest causes of death are almost invariably diseases of the lung, tubercle, bronchitis, pneumonia, and it stands responsible for from 25 per cent. to 35 per cent. of all deaths. No other organ or system can show a third of this fatality, the entire alimentary canal and its appendages, for instance, being responsible for less than 10 per cent. And the same disproportionate fatality is found in the lower animals. Percival states that in the horses of a cavalry regiment under his charge during ten years, nearly 60 per cent. of all deaths were due to diseases of the lungs, and all authorities agree that pneumonia is the most fatal of equine diseases, with glanders of the lung, a close second. Among cattle, tuberculosis and pleuro-pneumonia or cattle-plague head the list, the former causing as high as 40 and even 50 per cent. of the deaths in dairy cattle in some provinces. Nearly 40 per cent. of the monkeys and apes in the Zoological Gardens die of tuberculosis, and 30 per cent. more of bronchitis and pneumonia. Thirty per cent. of the carnivora die of pneumonia, and nearly 50 per cent. of the marsupials.

Whether this excessive vulnerability of the mammalian lung has any connection with the fact that it is by far the most recent of all our great vital organs, first appearing two-thirds of the way up our family tree in the lung-fishes, *Ceratodus* and *Protopterus*, is a question which has already been discussed in a previous chapter. Certain it is that recentness and instability go together, and that this part of our organism is less perfectly adjusted to its new environment, the air instead of water, than any other tissue. Indeed, the lung alveoli are the only air-living and air-breathing structures in our entire body, all the rest of our cells being still aquatic organisms and marine at that. They die unless kept flooded with salt water.

Professor MacFadyean accounts for the susceptibility of the lung to tuberculosis upon the purely mechanical ground that the infection entering through the alimentary canal is taken up by the lacteals, carried into the receptaculum chyli, and through this to the superior vena cava and right auricle. Thence it is, of course, pumped to the lungs, and their mesh being the first capillaries through which it passes, the bacilli naturally lodge there. But it seems hard to understand why at least as many of the bacilli do not get into the portal system instead of the lacteals, and lodge mechanically in the liver capillaries. And this explanation completely fails to account for the remarkable immunity of the bird's lung, when the abdominal viscera and lymphatics are simply packed with tuberculous material.

As to the curious immunity of the bird's lung in tuberculosis, it can only be said that it is in keeping with its low susceptibility to disease in general. Nearly all of the "plagues" and fatal diseases of birds attack only the abdominal viscera. I have found lesions of the lungs, of any sort, distinctly rare in necropsies upon birds at the Zoological Gardens.

The respiratory system of birds differs markedly from that of mammals. The lung is scarcely more than half the relative size, is extremely solid and vascular, and expands but little. A large part of the respiration is carried on by means of the huge air sacs, expansions of the bronchial and alveolar mucous membrane which fill the entire body cavity from clavicle to pelvis, and even extend into the shafts of the long bones. It would seem as if through them, many of the tissues took their oxygen at first hand instead of through the oxyhæmoglobin of the blood. In this respect they resemble the "invertebrate birds," the insects.

Whether these differences are adequate to account for the lower susceptibility of the bird-lung, would be impossible to say, but it would not seem improbable that this small, firm, vascular, inexpansile lung should have higher powers of resistance to bacterial invasion than the large, soft, comparatively anæmic lung of the mammal. Curiously enough, the bird-lung is in almost the same condition physiologically as the collapsed human lung, after Murphy's thoracotomy operation for the cure of localised tuberculosis.

This anomalous distribution might at first sight be explained by the growth-preferences of the avian type of bacilli, as Nocard's experiments have shown that if rabbits be inoculated in the usual way with avian tuberculous material, the abdominal type of disease is produced, while with human material the pulmonary type results; and the same is true in the horse, in the rare instances in which he can be infected by the avian bacilli. But as Nocard has also succeeded in changing both human and bovine bacilli into the avian type, so that they acquire virulence towards birds, by cultivating them in collodion capsules in the peritoneal cavities of successive fowls, this preference for the abdominal viscera would appear to be little more than an acquired habit of a germ compelled to live in bird-tissues.

It may, perhaps, be worth adding that although the lung proper of birds is comparatively seldom the site of disease, the other parts of the respiratory system, the great air sacs, are much more so. They are extremely prone to be attacked by pathogenic moulds, which form a thick layer over their surfaces, often making a complete cast of half their cavity and in some cases filling it up solidly. A thick whitish exudate, not unlike tough cream-cheese, is poured out from the walls, and upon this an abundant crop of white, green or black "mould-fur" grows, readily recognisable by the naked eye as well as under a lens. Among the water-fowl in the

Gardens more die of this aspergillosis than of tuberculosis, and I have twice found the trachea completely blocked by "emboli" colonies which had adhered to its wall.

Although we are unable to speak positively as to the precise method of the spread of the infection, yet fortunately, as to the practical steps which are to be adopted to limit its diffusion, there is no difference of opinion whatever. Even while giving first rank in importance and effectiveness to the defensive side of our campaign against tuberculosis, in the form of heightening by every possible means the general vigour, and increasing the natural resisting-power of the organism, yet our campaign, on the offensive against the spread of the infection, should be pushed with the utmost energy.

Among animals, where we are relieved from the more serious practical difficulties in the way of carrying out effective schemes for the prevention of the spread of infection and the isolation of infected cases, such as confront us in dealing with disease in our own species, the most gratifying and encouraging results have already been attained. Upon many of our most progressive and prominent breeding and dairy farms, both in America and upon the Continent, tuberculosis has been absolutely stamped out, and the stock kept free from it already for years, simply by first carrying out a rigorous weeding-out and destruction of all the members of the herd which reacted to the tuberculin test, and then by establishing a quarantine, or isolation pasture and sheds, in which all additions to the herd, by purchase, are kept under rigid observation from six months to a year after passing the tuberculin test, before being allowed to mix with the main body of cattle.

In Denmark a vigorous State-supported Commission, under the able leadership of Professor Bangs, has succeeded in stamping out tuberculosis, not merely in scores of herds, but in entire districts, and it is confidently expected that at no distant date the entire district will be free from bovine tuberculosis. One of the most encouraging features of this brilliant success is, that it has not even been found necessary to destroy all the infected cattle, but that pedigreed and other specially valuable cows may be preserved for breeding purposes, providing that they are rigidly isolated, and that their calves are removed from them immediately after birth, and brought up on the milk of non-infected cows. And as it is in high-bred dairy cattle that the disease is most frequently found, this possibility greatly diminishes the most serious obstacle to the carrying out of a vigorous system of this description, its enormous expense.

The difficulties in the way of carrying out any system of testing by inoculation upon most wild animals, the large proportion of them which are infected before their arrival, and the length of time which it would be necessary to keep them in quarantine, and consequently great demands upon their usually limited ground-space, have as yet prevented most of our Zoological Gardens from attempting any adequate scheme of this description. It is however reported as carried out with gratifying success in one of the smaller continental Gardens, at Schoenbrunnen, near Vienna. The mortality from tubercle among the monkeys in the ape-houses there, had become so enormous, that the directors determined some four or five years ago to destroy their entire existing stock, thoroughly disinfect the houses and cages, and make special arrangements to secure a new stock of monkeys and apes direct from their native forests. The greatest pains were taken to protect them from all possibilities of contagion on ship-board, and in transit generally. They were tested with tuberculin on their arrival at the

Gardens, with the gratifying result that not a single case of tuberculosis has been reported among them since. So that we certainly have every ground for encouragement to persevere in a vigorous effort to limit the spread of the infection in our own species, in spite of the immensely greater practical difficulties.

We are also, I think, justified in taking a somewhat more cheerful view than that usually held at present, as to the actual risk of communication of tubercle from animals to our own species. First of all we have the differences in type between the three forms of bacilli, which although not sufficient to distinguish them as separate species, are certainly adequate to considerably limit the possibilities of their transference to, and ready spread in, the tissues of an animal of a different class from that which they have habitually infested. The singular immunity of birds to both bovine and human bacilli, and of various animals to the avian bacillus, have already been alluded to, and while the opinion of the majority of veterinarians is strongly in favour of the frequent occurrence of direct transmission of the bovine form to the human subject, yet evidence is slowly accumulating, which we think would justify us in holding that there is at least a possibility of doubt on this question. Certainly, the most careful researches which have yet been carried out to determine this particular point, those of Dr. Theobald Smith of Harvard University, have led him to incline decidedly to the conclusion that the bacilli are not readily transferable.

While innumerable instances have been reported of the occurrence of tuberculosis in children and families, where the milk of a tuberculous cow has been used, yet it must be said, in fairness, that the more carefully these cases are investigated, the larger is the proportion of them which are found to present evidence of abundant opportunities for infection by the human germ. Indeed, one of the leading health officers of the State Board of Massachusetts, informs me, that in his experience, he has not yet been able to find a case in which he was perfectly satisfied that the disease in the human patient has actually been contracted through the use of infected meat or milk.

In the second place we have, in the case of meat, the valuable natural safeguard, that by a most fortunate coincidence, the one tissue which constitutes ninety-five per cent. of our food supply, the voluntary muscle, is the sole tissue in the body which is almost never attacked by tuberculosis. The tissues which are most commonly affected, the lungs, lymph-nodes and intestines, are extremely seldom used for human food, in fact, the only part of the body commonly so used, which is a frequent site of tuberculous invasion, is the liver. Then again, the thorough cooking to which ninety-five per cent. of all butcher's meat is subjected, will kill the bacilli in all parts, excepting the central portions of some large joints of meat, which regions are fortunately very seldom invaded by them, so that the leading veterinary authorities are gradually coming to the conclusion that the danger of infection from this source is not by any means so great as was at one time supposed. In the words of that most able and conservative comparative pathologist, Professor J. MacFadyean of the Royal Veterinary College, in an editorial in the *Journal of Comparative Pathology*, for September, 1898, "The investigations of the past few years and the Royal Commissions, which have reported upon the subject, have upon the whole tended to show, that the connection between human and bovine tuberculosis is not so intimate or so important as supposed. . . . . At least, with regard to the consumption of the flesh of tuberculous animals, there is a consensus of opinion that the danger is not a pressing one."

As concerns the danger of infection through milk, we cannot feel at all the same safety; yet even here we are entitled to a certain amount of reassurance. In the first place, tuberculosis of the udder is, on the whole, one of the rarer sites of the disease, and while it is possible for tubercle bacilli to get into the milk, directly from the circulation, without the udder being obviously affected, yet this must be regarded as a distinctly rare occurrence. Then, of course, we have the benefit of the doubt as to the possibility of the bovine bacillus readily finding a lodgment in human tissues, and although the researches of a number of observers, including the late lamented Kanthack, have disclosed the presence of tubercle bacilli in an alarming percentage of samples of milk and butter examined, ranging from ten per cent. to as high as twenty-five per cent., yet the question is still undetermined as to how many of these were of bovine, and how many of human origin.

Finally, as has already been stated, the remarkable immunity to tuberculosis possessed by the calf, even when fed upon infected milk, is entitled to some weight in this connection. Indeed, attention is already beginning to be called by veterinarians to this fact, as casting doubt upon the wholesale transmission of tubercular infection through milk, which was at one time believed to be possible. Professor Owen Williams, in a recent address before a Dairy Association, published in the *Edinburgh Veterinary Journal*, for May, 1899, specially emphasized this fact, citing the statistics of German slaughter-houses, showing a rate of less than 1 per 1000 in young calves, and seriously doubting whether milk was often a source of infection, especially in view of the abundant possibilities of contagion through other channels.

Moreover, we have the broad and consoling result of actual experience, that while the consumption of both meat and milk *per capita* has enormously increased during the past thirty years, the death-rate from tuberculosis has in the same time decreased nearly 40 per cent. Either these foods are not an important source of infection, or their effect upon the vigour and resisting power of the race has overwhelmingly over-balanced the dangers from their use.

The only even apparent exception to this statement, is the unfortunate allegation of Sir Richard Thorne in the *Harben Lectures* for 1898, to the effect that the death-rate from "tabes mesenterica," or tuberculous enteritis, in children had increased, which he attributed to the much greater use of milk as an infant food. This statement has, however, been simply riddled by one pediatrist and pathologist after another, beginning with Mr. Walter Carr in the very next number of *The Lancet*,* rapidly followed by Drs. Guthrie, Still and Donkin. These authorities were practically unanimous in declaring upon the basis of carefully tabulated researches, that the condition usually described under the name "tabes mesenterica" is, in the great majority of cases, not tuberculosis at all, but only chronic gastro-intestinal catarrh; that tuberculosis of the abdominal viscera is a rare cause of death in children; and that the disease begins in the abdomen far less frequently than in the thorax.

In 120 cases of tuberculosis in children, reported by Walter Carr, and 46 by Dr. Still, or 166 in all, in which

* Vol. II., 1898, p. 1662.

the starting-point of the disease could be determined *post mortem*, this was in the thorax in 105, and in the abdomen in 36, and the younger the children the more marked was this preference for the lung.*

Nothing could be further from my purpose than to urge these considerations of probable natural safeguards, as ground or even excuse for any slackening of our efforts to secure a complete and universal system of tuberculin-testing in dairy-cattle, and a rigid inspection of all stock-yards, slaughter-houses, and carcases. We should not tolerate for a moment the use as human food of either the meat or milk of animals suffering from any serious disease, whether infectious or not, nor can we afford to run any risk which is so clearly avoidable.

Great as the expense of such a system must be, this would be mainly *first outlay* only, if at all reasonably successful, and it is difficult to imagine any better investment on behalf of the community. By all means stamp out the bovine disease, and by every reasonable and humane means in our power limit the spread of infection in our own species, but let our chief object and reliance be the development of a carnivorous degree of resisting power in the human organism. To this has been due the lion's share of our success hitherto, and, like all of nature's safeguards, it will form our most lasting and only permanent defence for the future.

* Walter Carr, *British Medical Journal*, Sept. 2nd, 1899.

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