The origin of disease : especially of disease resulting from intrinsic as opposed to extrinsic causes : with chapters on diagnosis, prognosis, and treatment / by Arthur V. Meigs.

THE

ORIGIN OF DISEASE,

ESPECIALLY OF

DISEASE RESULTING FROM INTRINSIC AS OPPOSED TO EXTRINSIC CAUSES.

WITH

CHAPTERS ON DIAGNOSIS, PROGNOSIS, AND TREATMENT.

BY

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WITH ONE HUNDRED AND THIRTY-SEVEN ORIGINAL ILLUSTRATIONS.

SECOND EDITION.

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TO THE MEMORY

OF

RICHARD BRIGHT,

AND OF

WILLIAM WITHEY GULL AND HENRY GAWEN SUTTON

WHOSE JOINT LABORS HAVE SHOWN
BRIGHT'S DISEASE
TO BE A WIDE-SPREAD PROCESS, RATHER THAN A
DISEASE OF THE KIDNEYS,

THIS BOOK

IS IN ADMIRATION DEDICATED.

PREFACE TO THE SECOND EDITION.

It is highly gratifying to me that my book was received with such favor that in less than two years the first edition has been exhausted. For fifteen years my energies were directed towards gathering and arranging my materials. In writing I have endeavored to record my observations of nature apart from my opinions, because a careful record of facts may be of permanent value, while opinions are liable to change. I would direct special attention to the illustrations. In their preparation the utmost care was exercised to make them true to nature, and of microscopical preparations only those were used in which the outlines and topographical relations could be distinctly seen. I am grateful for the consideration that has been shown me in the reviews, almost all of which have seemed to realize the difficulty of my task and have recognized that its accomplishment involved great and protracted labor. Parts of what I have written are not in agreement with doctrines now generally accepted,—for instance, that in regard to the cause of consumption of the lungs. The reception accorded my book has encouraged me to think that a larger part of the medical profession than a superficial examination would indicate may still remain unconvinced that the causative agency of the bacillus tuberculosis has been logically proved. That portion of the chapter on the heart which deals with anatomy has been entirely rewritten and new drawings have been introduced. The new pictures demonstrate more perfectly than the old ones both the penetration of the muscular fibres by the capillaries and the character of the large capillaries which are peculiar to the heart. New plates have been made for five of the photographic process illustrations, the old ones not having been entirely satisfactory. A few errors in the text have been corrected.

July 10, 1899.

PREFACE TO THE FIRST EDITION.

MUCH of the progress of medicine in the past fifty years has been due to specialism. Well-qualified men have devoted themselves to restricted fields, and important discoveries have been made that would not have been possible had they extended their labors more widely. The advantages of specialism are patent; but it is certain that a wide divergence of knowledge also results from it, and that facts which belong together are often observed by persons whose lines of research lead them so far apart that for a long time the conclusion remains undiscovered. There is great need for something to counterbalance this inevitable evil result, and to bring together the facts which isolated are useless. The relation of clinical medicine with pathology is obvious, and there can be no doubt that they are separated to the disadvantage of both. Specialism therefore has gone sufficiently far, if not already too far, in medicine, and it is time that something be done to connect the various disjointed threads of knowledge, the true value of which can never be known until they are woven into a complete whole. Impressed by the separation of clinical medicine from pathology, I have endeavored to bring them nearer together, and my book is the result of that effort.

At autopsies in hospital practice it has been my custom to retain for microscopical examination portions of the five great organs,—heart, lung, liver, spleen, and kidney,—and of any other tissue the appearance of which seemed to indicate disease. The habit of examining with the microscope portions of the five organs named, even if no disease was apparent to the unaided eye, has been prolific of result. It is common for lesions which entirely escape the closest macroscopic investigation to be revealed by the microscope. Thus by examining tissues revealing no unhealthy appearance, the beginnings of disease can be studied.

It is often difficult to determine whether an unnatural condition that is seen with the microscope is due to post-mortem change or bad

technique, or is actually disease. This difficulty I have endeavored to reduce to a minimum by pursuing a uniform method of fixation of tissues and of preparation of sections. Small pieces of all tissues to be examined with the microscope were cut at the time of the post-mortem examination and at once placed in seventy per cent. alcohol, which was frequently changed during the first forty-eight hours, except in the case of nervous tissues, when Müller's fluid (solution of bichromate of potassium and sulphate of sodium) was used. Paraffine has been the embedding material, and carmine the stain. A carmine solution of uniform strength was used, and the tissues kept in it for a certain length of time. The color is an important matter, for the condition of tissues is often judged by the way in which they take the color or remain unstained. Besides the method of examination that has been described, others have been used when the occasion seemed to demand it.

The pursuance of a uniform plan of examination is most important, for after a sufficient degree of experience has been attained it is possible to make a reasonably certain distinction between disease and changes due to other causes.

In elaborating my work it was necessary to make the argument as complete as possible, and no great number of quotations could be included, nor many references. This may sometimes make it seem as if it is intended to claim as my own observations that were made by others, which is not my intention; all that is claimed being that the general thread of the argument and the conclusions are my own. These are necessarily based, to a great extent, upon the observations of others, although there are a good many facts that are new and have not been previously recorded, especially in regard to microscopical pathology.

The one hundred and thirty-seven illustrations are all original, and were made by Mr. Hermann Faber and Mr. Erwin F. Faber. It would be impossible to exaggerate the faithfulness and skill with which they have performed their work. All but one of the pen-drawings are by Mr. Erwin F. Faber, and the etchings on steel are partly by one and partly by the other of the artists. The sections of tissues are, with two exceptions, my own preparations. The drawings were made with the camera lucida, the outlines, dimensions, and relations of parts being thus kept true to nature. With each picture is a scale, magnified to the same extent as the tissue, which enables any one to ascertain the enlargement. The method, so far as

concerns the etchings, has probably been seldom if ever previously employed. The reflection of the magnified object was thrown by the camera lucida upon the steel plate and traced directly with the needle by the etcher, thus obviating the necessity for the intermediate sketch which is ordinarily used in etching. For accuracy this method cannot be surpassed.

In the Pennsylvania Hospital, with which institution I have been connected almost continuously in one capacity or another as physician for twenty-five years, I have enjoyed almost unlimited opportunity for study. Only those who have been associated with hospitals can appreciate the gratitude and loyalty felt by a physician for the institution which has rendered him this invaluable service.

Throughout my work, from its conception to the printing of the last page, I have been aided by my friend Dr. Harvey Shoemaker. Beginning as my assistant in the hospital, he has continued to afford me help at every stage in the construction of my work. I owe more than I can express to his kind sympathy and good advice.

This preface must not be closed without including an acknowledgment of the services of Mr. Joseph McCreery. Through his learning and by his fidelity in reading the proof-sheets he has eliminated many errors from the text.

May 19, 1897.

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INTRODUCTORY.

In the earlier part of my work as a hospital physician, finding myself without any understanding of microscopical pathology, and with but an ordinary and superficial knowledge of the gross appearances of disease, the results of my labors were exceedingly unsatisfactory and disheartening. The portion of the work in a hospital ward which consumes the greatest amount of time is diagnosis, for after that is once made prognosis almost speaks for itself, and treatment, although the most important part of the science of medicine, is in most cases simple, and its direction takes but little time, if it is possible to feel assured in the diagnosis. Ward work pursued with little understanding of gross and none of microscopical pathology soon became so unsatisfactory to me that it was insupportable. The accepted views of disease lead to a degree of precision in their classification that accords ill with the lesions found if the study of cases is pursued beyond the field of clinical medicine into pathology and the results studied as a whole. Most cases are named with precision as being disease of one organ or another. This may be a sufficiently good way for the pathologist who can work at his leisure and in turn study the various different morbid conditions to which the heart, kidney, or other organ is subject, for it is unnecessary at the moment that he should consider either the fact that in most cases more than one organ is involved or the relations of lesions of different organs one with another. For the hospital physician, however, who studies pathology in the cases he fails to cure, the classification of disease by single organs is almost useless.

The result of some years' study in a hospital, including attendance at the post-mortem examinations, convinced me that to have any real

grasp upon the management of disease it is absolutely necessary to be equipped with sufficient understanding of pathology to be able to follow that side of medicine. Study pursued in this way, in private practice and in the wards of a hospital, followed, whenever the opportunity offered, into pathology, has resulted in the conviction that many diseases usually considered as confined to one organ are seldom so confined, for there are lesions of other organs that are just as definite as those of the part considered to be the seat of origin. At the same time, many of the lesions are of such nature as to render it certain that they existed before the onset of the fatal attack. This is, of course, much more the case in chronic diseases than in those which are acute, and especially than in those which are acute and certainly of extrinsic origin. These two facts—the multiplicity of lesions throughout the body in diseases commonly looked upon as being of one particular organ, and the frequency of lesions that long antedate the fatal attack —are of the very greatest importance. They point to a mode of origin of disease which at the present day does not receive its due share of attention.

For practical purposes of discussion all diseases may be divided into two classes,—those of extrinsic and those of intrinsic origin. Types of the former are small-pox and measles, which are caused by poisons that pass from one body to another. The contagious entity to which such diseases are due is as much a thing apart from the human organism as a bullet which kills a man shot through the brain. The fact that the real nature of such poisons is absolutely unknown, whether they are solid, gaseous, or of some composition as yet beyond our understanding, does not lessen the certainty that the cause is extrinsic. As a type of disease of intrinsic origin may be mentioned the formation of cysts in the kidney, which is so common a process in the aged and in those suffering with contracted kidney. It is the result of abnormal action on the part of the organism, and is entirely independent of the direct action of any extraneous cause.

That the causes of disease are so divided into two classes no one will deny, for it is self-evident to all who have reflected upon the subject. Although it is easy to recognize types of the extremes of the two classes, it is often difficult or impossible to decide how to classify individual diseases, for with disease, as with almost everything else in nature, there are no abrupt lines. Every known disease has a place somewhere on the long stretch that reaches between those certainly of extrinsic and those of purely intrinsic origin. In the middle,

however, between the two extremes, there exist diseases which undoubtedly have their origin in a combination of both extrinsic and intrinsic causes. Many others exist whose mode of origin as yet remains unknown or is in dispute, it being sometimes said that they arise from the action of a poison, or, again, that they are the result of misdirected growth or of degeneration.

Disease should be looked upon as a complete whole composed of very heterogeneous elements. The differences of these elements at the extremes are radical and easily recognized, but in the ordering of diseases Nature has followed her usual plan and drawn no lines to separate them into sharply defined classes. At one end the diseases of positively extrinsic origin are shaded toward those which arise from within, owing to the poisons being more and more subtle in their action, until finally it becomes impossible to ascertain whether there is any extraneous cause working to produce a particular condition. At the other end, from diseases certainly of intrinsic origin we reach gradually others which are complicated by the operation of external causes until they, too, can no longer be satisfactorily classified. Thus, from the two extremes of disease of extrinsic and of purely intrinsic origin both approach a common centre, becoming gradually in their progress more and more alike, until finally all distinction is lost and there are found to be many diseases which owe their existence to the double action of causes acting from without and from within. Such a division is a natural one, for it is certain that much disease is due to causes external to the organism, and it is equally sure that mere age will produce decay and degeneration, for the very rocks disintegrate with the passage of time. The division also is sufficiently comprehensive to include all diseases. It must be confessed, however, that it is often impossible to decide where between the two extremes particular forms shall be placed. No classifications used by naturalists are complete, for all of them can be shown to be imperfect, if not actually unreasonable, in some particular, but if they afford us a means to place collections of abstract or concrete things in an orderly manner for use, their purpose has been served, and they may remain until superseded by something better. Even the division of disease into two classes is in some respects imperfect, for the causes of disease, as well as the diseases themselves, cannot be sharply divided, and there is a middle ground for doubt or dispute. If a man is struck upon the head with a hammer, the result is degeneration or destruction of the part injured. Is the cause here an extrinsic or an intrinsic one? There

has been nothing of the influence of a poison to produce the result, nor could it be charged to any abnormal action of the organism itself. The state of the atmosphere, also, often operates to the production of disease. In this case the mode of causation is even more complicated and impossible of definite explanation, for besides the capability of the atmosphere to produce results similar to those of a blow, as, for instance, the effects of sufficiently low and high temperatures, it is well known that the air often carries in it both solids and liquids which can be compared only to poisons in their injurious effects. When the atmosphere does cause disease it is often impossible to ascertain in which of these two ways the result has been brought about. The results of an injury like a blow, or the harm done by atmospheric conditions, could not be thought to be caused by a poison or to be due to any disordered action of the bodily mechanism, but the condition of the tissues that they produce is much more like what results from the passage of time than like the ordinary effects of poisons.

My intention is not to write a complete treatise upon the causation of disease, but only to describe and comment upon certain observations. What has already been said has been for the purpose of expressing in brief outline views which are universally held in regard to the origin of disease, avoiding everything in regard to which there might be controversy. My observations have led me to believe that many diseases originate in a manner different from that commonly supposed, and that there is often a connection between morbid processes which are ordinarily thought to be unrelated. The sources of these observations have been three,—private practice, ward work in a general hospital, and the study of pathology.

Private practice renders possible the study of individual cases for many years continuously. The antecedent period, the beginning of disease, its progress and end, may all be followed. If the end is death there is sometimes also the opportunity to study pathology, and under such circumstances is obtained the most complete knowledge of a disease that it is possible to have. In private practice it is occasionally seen that chronic diseases usually supposed always to terminate fatally may last for many years and finally be recovered from, or, at any rate, the patient continue in such good general health that for all practical purposes he may be considered to be well. This is especially common in cases of chronic lung disease of such nature that it is impossible to say they are not tubercular, and in affections of the kidney which have been called Bright's disease, and which a few years ago it was

thought always proved fatal in about two years. The largest private practice, however, yields but a small field for the study of clinical phenomena in comparison with what is obtained in the wards of hospitals. In them are grouped vast numbers of cases, the greatest portion of which are of serious nature, for but few persons suffering with the more trivial ailments and diseases find their way into hospitals. Besides, the patients in hospital wards are almost universally of the lower classes, and in such people all diseases which tend to recur are liable to be of more severe form and of more rapid recurrence than among those of the better class. The lower classes are so much exposed to physical hardships, and owing to their poverty are so often forced to take up their labor again after an attack of illness before having had sufficient time to recover fully, that their condition as seen in hospital wards presents a picture which has no parallel among persons of the better class who are not subjected to such exposure. In them diseases of the heart, lungs, liver, and kidneys, which involve the existence of great degrees of inflammation, recur with a rapidity and virulence that are surprising, and it is common for persons suffering in this way to return two or three times to a hospital within a short period and die. It might well happen to an observer of disease whose studies were pursued in the wards of a general hospital, where the number of chronic cases and of recurrent diseases is always so great, to exaggerate the importance of intrinsic causes, which play so large a part under those circumstances, and to underestimate the effects of extrinsic causes. If such has been my error, it finds its excuse in the natural reaction from the common overestimate of the importance of poisons in the causation of disease. This is often so greatly stretched that, if no semblance of an extrinsic cause for a particular disease can be found, the extremists assume that the poison must exist and will some day be discovered, and then build theories upon the assumption.

It is a striking fact that human beings are much more liable to disease during early life and when they have become old than in the middle period. This peculiarity is common to the whole organic kingdom, being the rule among the lower animals and even in plants, just as with human beings, who represent the highest type of organization. The reason for the excessive mortality in infancy and early life is in a way easy to understand, but, on the other hand, no single physical cause for it can be discovered which is parallel with that which explains death in the aged. In aged beings death seems

natural, for all the parts of the organism become worn out, but with the death of young creatures there is always connected a feeling of sadness, as though some injustice had been done and with a better opportunity the calamity might have been avoided. In the young decay and degeneration seem out of place. Until adult life is reached the tendency is entirely the other way, the natural inclination being toward perfection, repair is easy, and growth goes on until the full size has been attained. During the whole period of growth the capacity to overcome the ill effects of any injury received is immense, for so long as growth continues new tissue is produced, and this is generally uninfluenced by injuries antecedent to its existence. In early life the tissues are soft and succulent, contrasting strongly with those of age, which are dry and brittle. They are prone to active inflammation, which, however, is seldom of long duration like inflammation in the old, in whom it tends to become chronic. The inelastic and hard tissues of the aged are disposed when once inflamed to continue in a slow or latent state of inflammation. The inclination in youth is toward repair, and this is especially strong up to the time when full size is attained, and the natural end of disease or inflammation in the young is healing, if the damage is not irreparable. In considering, however, the origin of disease, it must not be lost sight of that attacks of sickness or injuries received in early life may often lay the train for future outbreaks. It is not rare that the seed of disease is planted by some attack in infancy or childhood and after lying dormant for years develops in middle life or old age. This peculiarity will be fully discussed later. The diseases of extrinsic origin flourish during early life. It seems as if the nature of the tissues invites the operation of all the extrinsic causes of disease, and especially those which are truly contagious are readily passed from one body to another. On the other hand, the fully developed tissues of the adult period are comparatively non-receptive, and in old age disease of extrinsic origin reaches its minimum.

At first thought it would seem impossible for two things to be farther apart or less related to each other than youth and age. They are the extremes of life, and under natural conditions, if no obstructions fall in the way of physiological development, have nothing to do with each other, but remain always far apart. Disease accomplishes what might well be thought impossible: it forces the two together, and for the pathologist there is produced the strange paradox of the commingling of youth with age. To the physiologist such an assertion

may seem absurd, and, if the words youth and age are held strictly to their meanings as applied to the length of life of beings, to be impossible. If, however, the subject is considered from the stand-point of pathology and the condition of the tissues examined, the meaning of the assertion that youth and age may be mingled will be understood, and it will be perceived that disease can so far change a being young in years as to produce all the conditions which under natural circumstances are found only in the old. The mingling of youth with age is the consequence of premature age in youth, and not of anything like a postponement of the natural effects of time, which could result only in something like immortality, a thing which in the present state of knowledge seems impossible. This subject is one of great importance, and when correctly understood it will be seen to be a potent factor in the origin of disease.

CHAPTER II.

THE DISEASE OF AGE.

As time elapses the human tissues become stiff and brittle, fat accumulates, and there is a great increase of the amount of fibrous tissue. It is, however, by no means solely the number of years a human being has lived that makes him appear most nearly typical of youth or of age. Some seem born to live long lives and to enjoy a green old age, looking more youthful at seventy than many children prematurely old from disease. Such children become wrinkled and old-looking while yet in the earliest years of life, and die, as fruits dry and shrivel and fall to the ground, useless before maturity. It is not intended to express any doubt as to the existence of a healthy old age, or to assert that all men old in years are necessarily diseased. Nevertheless, the pathological changes about to be described inevitably show themselves sooner or later in the tissues of all men who live long enough for them to develop. Otherwise, if the various accidental causes of death could be escaped, there would be no limit to the duration of life, and even immortality would be theoretically possible. It may be said that the human machine must wear out and become incapable of further work within one hundred years, and this natural termination of the life of man is as inevitable as is the death of certain plants after they have performed their function in the world by producing flowers and perfecting seed. In man, as in the plant, the period of extinction is, within limits, variable.

The period at which the body begins to show the disease of age differs greatly; often it is premature, owing to imperfections or to great wear and tear produced by dissipation, excessive labor, or some unhealthy mode of living. In making post-mortem examinations one is often surprised at the extremely old appearance of the body of a child, and again at the softness and pliability and generally youthful appearances presented by an old man. It is well known that at birth, and even during embryonic life, fibrous tissue exists in the form of tendons and other necessary portions of the supporting framework, and that a moderate amount of fat is also to be found.

The question of the significance of fat is one in regard to which

there is room for the greatest difference of opinion. In every human body there is more or less adipose tissue, and it would be unreasonable to say that fat is always a product of disease, but that it does often accumulate to such an extent as to be pathological is undeniable. Every physician of experience has met with cases of so-called Bright's disease in the course of which, during the downward progress toward death, either an enormous accumulation of fat developed or the patient became exceedingly emaciated. In such cases albumen and casts are present in the urine, and the degenerative process involves in greater or less degree other great organs as well as the kidneys. When during the last few months of life an enormous increase of fat takes place, the patient growing in weight by from twenty to fifty pounds and still becoming weaker and more short of breath and oppressed by his own unwieldiness, it is evident that this growth of adipose tissue which insinuates itself into every space and fills every cavity to bursting is morbid. If a man at sixty weighing one hundred and seventy pounds begins suddenly to gain and in the course of a year or two reaches two hundred and ten, meantime becoming visibly and rapidly older in body and mind, it is only reasonable to class the condition as one of disease. Such a change during the latter part of life is not rare, and persons so affected become mentally incapable of sustaining that which was formerly easy to them. The ordinary affairs of life become burdensome, they fear responsibility and avoid it, and when unable to avoid it do ill that which formerly they did well. In function the digestion becomes weak and they are prone to have diarrhœa or to be constipated, they are short of breath, and frequently take cold, or are very rheumatic. The end comes with an apoplectic seizure, dropsy, subacute pneumonia, or some other apparently acute condition whose foundations were laid in the invisible changes that occurred in the organs coincidently with and as a part of the visible increase of fat.

This sudden accumulation of fat during the latter years of life is difficult to comprehend, and at the present time it is impossible to give any facts showing definitely its meaning; but it would be unreasonable to deny that it constitutes a part of a disease, if not actually an independent disease in itself.

The morbid increase of fibrous tissue is one of the most interesting and important phenomena presented to the mind of the discriminating pathologist. The tendons, the supporting material in the interstices of the kidneys and liver, and the perivascular connective tissue are

types of the fibrous tissues known to histologists, but they bear little resemblance to that which forms as the result of disease in the organs and elsewhere. This morbid growth, which insinuates itself into so many places where it has no natural home, is hard, dense, and unyielding when compared with the soft and pliable organs in which it is found; and that it is properly named fibrous tissue may be doubted, or with reason denied altogether.

Many arguments might be adduced favoring the belief that morbid fibrous tissue is a thing entirely different from healthy fibrous tissues, but, as it would be impossible now to bring forward facts sufficient to prove the accepted opinions incorrect, it does not seem worth while to enter into a very full discussion of the subject.

As life advances, new adaptations and changes are constantly occurring, and from the earliest embryological periods to the most extreme old age these continue without any periods of rest, but with the greatest apparent variation in the rate of progress. Sometimes, as already said, an old man preserves his youthful appearance, and, again, an infant may caricature the appearance of age. The changes in the skeleton have been studied and are well known. The skull grows thick and increases in weight, the thigh-bones lose much of the cancellous tissue, are lighter, and ill adapted to bear strain and violence, and there are other changes that are well known.

An interesting feature in this connection is the increasing complexity of anatomical structure as age advances. Nothing could be simpler in form than the primitive ovum, and yet no machine has ever been constructed which is so complex in its arrangement as the adult human organism. The increase of this complexity can be followed to a certain extent, and the reason for its existence can be easily seen in some cases, while in others none is apparent. As an instance of the first may be mentioned the nervous system, which begins as a shallow furrow upon the dorsal surface of the embryo. It then deepens and finally closes at the top, thus becoming a hollow cylinder. Later the walls of the tube increase in thickness at the expense of the cavity until a solid rod is formed, and meantime it has turned and folded and bent itself in many directions and at many places until there has been formed from so simple a beginning the marvellously complex human brain and peripheral nervous system. The reason for the complexity of structure here exhibited is easy to comprehend, for there is no other known instance in nature of so complicated an organism being packed in so small a space. The

second proposition is illustrated by the developmental anatomy of the kidney. It is well known that the Malpighian bodies lie upon both sides of the bundles of straight tubules (the pyramids of Ferrein) which extend outwardly from the medullary region to the capsule. In early infancy they are grouped in such a manner as to present the appearance of a tree with its branches, with fruit hanging at their ends. The simplicity and beauty of the arrangement are such as at once to catch the eye. At a later period, however, during adult life, this arrangement has disappeared, or at least can no longer be seen, and apparent confusion has taken the place of the former simple order. The Malpighian bodies appear to have increased greatly in number, they crowd closely upon the straight tubules, and are scattered without apparent order throughout the labyrinthine regions. The beautiful appearance of curving branches with fruit hanging at their ends can no longer be seen.

The painful joint-affection of the aged called rheumatism, in the course of which fibroid material increases and earthy salts are deposited in and around the articulations, is so often an accompaniment of age, and so commonly looked upon as inevitable, that it is not unusual to hear aged people express thankfulness at their freedom from pain if they chance to escape this particular infliction. This so-called rheumatism of the aged, so far as the anatomical alteration of the joints is concerned, appears to be of the same nature as the process which shows itself by the deposit of fibroid material in the organs, differing only in the locality affected. There is the same slow inflammation with alteration of the part invaded, the new material deposited being useless, if its presence in the place into which it may have intruded does not become actually injurious. If this view is correct, it will be necessary to rearrange somewhat our views about rheumatism. Either that which has been called rheumatism in the aged is not rheumatism at all, but is a form of fibrosis incident to age, or else all varieties of rheumatism are of this nature, and are to be classed as species of degeneration. Strange as such a doctrine may at first sight be thought, many facts might be adduced which lend it strong support. The acute inflammatory rheumatism of young people does not at a cursory view present any resemblance to the painful and distorted condition of the joints so common in the aged. Acute rheumatism is peculiarly the disease of those who are exposed to dampness and wet, notably sailors, and it is at first, so far as at present known, nothing but an acute inflammation which attacks the joints

and the heart. One of its marked peculiarities is its aptitude to recur, especially if the mode of living which precipitated the first attack be continued. Those who have been much with sailors think them short-lived and that they become disabled and grow old early. First attacks of rheumatism in young people are most commonly of the acute variety, and when the attack has passed away the individual is left as well and active as ever. Later there will be another acute seizure, or perhaps after an interval of perfect health an attack of subacute rheumatism of the knees or ankles or other joints. During the subacute attacks there is generally no fever, and no disability except that caused directly by the local affection of the joints. There is none of the general bodily sickness and prostration which are invariable accompaniments of acute rheumatic fever. It is not necessary to describe the bodily condition of a rheumatic old man, nor is it needful to say that all possible gradations of change of the joints occur, from that which is seen in the most acute variety of rheumatic fever in a young sailor to the so-called rheumatism of the octogenarian. No one has ever been able to point to a distinct division in the line which has at one of its ends acute rheumatism and at the other chronic rheumatic synovitis. The two are beyond doubt nearly related to each other; they are at most only different species of the same genus. If this is allowed, and it is conceded that the rheumatism of the aged is a degeneration, a form of fibrosis, and a part of the process which occurs in the organs of all men as life progresses, then it follows that acute rheumatism is in some wise of the same nature. There is, therefore, much reason to think that all rheumatism is degenerative, and that it is but one of the parts of that which has been called the disease of age. This statement may seem untenable, if not almost absurd, if it be considered from the side of our experience of acute rheumatic fever alone. More careful consideration of the facts, however, makes it clear that chronic synovitis is a degeneration, and of the same nature as or allied to fibrosis of the organs; and, this being true, there is no escape from the conclusion that all varieties of rheumatism belong in the same category, however unlike the extreme youth of the disease, which is acute rheumatic fever, may be to its old age, which is chronic rheumatic synovitis.

The influence of injuries and disease upon the prospects of longevity is a problem of great interest and importance. It is probably strictly true that no morbid process involving the existence of inflammation ever takes place without leaving the part attacked in a more or less

imperfect condition. Every tissue which has been subjected to the malign influence of inflammation, beyond the earliest and slightest stage of congestion, is left somewhat scarred. There are scars of all degrees, from the slightest condensation of tissue which can be discovered only by careful microscopical examination, to the tough and contracting material which results from attacks of pleurisy. It does not seem to be overstepping the limits of truth to say that every sickness which occurs during life bears with it more than the mere danger of the moment, and is an injury, which must leave the individual in a state more or less removed from physiological perfection.

Fibrosis, which is the growth and increase of morbid fibroid material, is the essential pathological change incident to age: it is the "disease of age." In all those who live beyond the ordinary term of life, excess of fibroid tissue develops, and, if no accidental cause of death steps in to close the scene, this degeneration finally reaches a stage when life can no longer continue. The parallel between the old man and the ancient tree is trite, but it is none the less apt. A resemblance can be conjured up in almost every respect between the bodily condition of the aged man and the old tree with its hollow trunk and its few remaining branches of rotten wood, which is brittle, soft, and lifeless, without sap, and unable to resist strain.

Among all the diseases received into the modern classifications there is none which comes nearer to this "disease of age" than what has long been named Bright's disease. Bright's disease of the contracted form, with the morbid conditions which are connected with it, is identical with what has been described in the foregoing pages. Contracted kidney, as is known by every one, is associated with enlargement of the heart and disease of the blood-vessels, with disease of the spinal cord and brain, with bronchitis, emphysema, and the slower forms of pneumonia, and with liver disorders. An important lesion, if not the essential one, in all the parts involved is an accumulation of morbid fibroid tissue. It is a matter of common knowledge that old people are prone to have fibroid and cystic kidneys, and that the heart is larger than in youth, though no one would presume to say that it is stronger. The stiffened arteries of age and the bronchitis which carries with it emphysema are so well known as hardly to need mention. All human beings, then, who do not die from some other cause develop fibrosis, which progresses with greater or less rapidity until the organism is so far injured that something must give way; then the machine stops. This is as true of man as it is of the

trees, which are certain to grow old in appearance and in fact, and with them age constitutes a disease which produces alterations in many respects parallel with the fibrosis of man.

Age in mankind, however, if it is to be looked upon as a disease, makes its appearance at no fixed period. There is no other animal that is subjected to such an infinite number of variations in its methods of living as is man. Man lives in every climate where any mammal dwells; his houses are of every conceivable gradation, from the palaces of Europe and the East to huts so miserable as to afford less shelter than the dwellings of many of the lower animals. His clothing and work and the food and drink upon which he subsists could not be more varied. Owing probably to his widely differing environments, man shows the greatest variation in the age at which he appears to grow old. If this question of age be looked at from a point of view more comprehensive than that of the external appearance of the aged and the number of their years when they die, if it be examined with the aid of the light thrown upon it by the science of pathology, many things of great interest will be developed, things that may aid in building up knowledge that shall enable us to put back the period of death even farther than has yet been possible. The opportunities of man to disregard the rules of hygiene and to indulge in practices which tend to shorten life are very much greater than those of any of the lower animals. No one of the lower animals cooks its food or partakes of alcohol. Man does both; he eats a variety of food and an amount ill adapted to his mode of life; he eats many things that under all circumstances are unwholesome; and he frequently takes a quantity of alcohol quite incompatible with the continuance of good health. As a consequence he is liable to suffer ills that have no parallel either in the lower animals or in vegetable life. Fibrosis, therefore, that which has been suggested as essentially the disease of age, is quite common in middle age, and even in youth, presenting, so far as the pathological conditions are concerned, exactly the same appearances as are found in those old in years. It is apparently the result of dissipation or overwork, or is due to inherited tendencies, such as are transmitted by syphilis and tuberculosis, or to any combination of these causes. Man, then, owing to his mode of life, may die at any age, even in youth, of a disease pathologically the same as that which must eventually prove fatal to all men who escape other diseases and accidental causes of death. As a result of inherited tendencies, its signs often appear very early, probably even during the embryological

period. Bright's disease of the more chronic forms, especially contracted kidney, with the wide range of symptoms and many pathological lesions which are grouped with it, is the type of the *disease of age*, whose essential features are fibrosis and certain changes in the blood-vessels. It is impossible at present to determine whether the blood vessel changes antedate the fibrosis and are its cause, or whether they are its consequence; or, on the other hand, whether the fact that the two are always in company is to be considered as a mere coincidence. The last possibility is in the highest degree improbable.

In his book "Old Age," George Murray Humphrey* attempts to show that there is a such a thing as physiological death, and much is adduced which is very interesting and instructive concerning the life and death of aged people. Some idea of the views of this author may be had from the following (page 5 *et seq.*): "It may be said, indeed, that at all periods of life the healthy and well-working, and especially the enduring, quality of the body depends upon a good adjustment, a good balance, of the several parts; and it is upon the well-ordered, proportionately or developmentally regulated decline in the several organs that the stages which succeed to maturity are safely passed, and that crown of physical glory, a healthy old age, is attained.

"A time comes at length when, in the course of the descending developmental processes, the several components of the machine, slowly and much, though equally, weakened, fail to answer to one another's call, which is also weakened; a time when the nervous, the circulatory, and the respiratory organs have not force enough to keep one another going; then the wheels stop rather than are stopped, and a developmental or physiological death terminates the developmental or physiological decay. The old man who had gone to bed apparently much as usual is found dead in the morning, as though life's engine had been unable to repair itself in sleep sufficiently to bear the withdrawal of the stimulus of wakefulness. . . .

"How much may those who pass gently into this natural and physiological death be envied by the many sufferers under the protracted and painful pathological processes which too often induce a premature extinction of life! . . .

"Yet, strange and paradoxical as it may seem, this gradual natural

* Old Age, by George Murray Humphrey, M.D., F.R.S., Cambridge, Macmillan & Bowes, 1889. Chapter I. is the Annual Oration delivered before the Medical Society of London, on Monday, May 4, 1885.

decay and death, with the physiological processes which bring them about, do not appear to present themselves in the ordinary economy of Nature, but to be dependent upon the sheltering influences of civilization for the opportunity to manifest themselves and to continue their work. For the needs of the first or infantile period of animal helplessness Nature has made a sufficient provision in the parental instinct which protects and nurtures the young. But this lasts only so long as the requirement for it exists. It ceases as soon as the young animal has the ability to help itself; and it does not return, and is not supplemented by anything of its kind. It gives way before that struggle for existence which is the engenderer of selfishness, which dominates over all other impulses and shuts out all heed for the worn and weary, for the feeble and the decaying. These, being unable to help themselves, are crushed out by the various provisions which Nature makes for their destruction. The good result of this great seeming evil is that all in the natural, or primitive, animal world is in the ascendant to, or in the enjoyment of, bodily perfection. . . .

"The same with disease. It, in like manner, stops itself. Indeed, it can scarcely be said to be allowed to enter into the pure realm of Nature. Sick animals are not there provided for, have no abiding-place there, and soon perish; so that there is no wasting and pining, no lingering fevers, no destroying cancers, no decrepit frames. Neither the bird that fails to elude the hawk, nor the hawk that fails to seize the bird, can long continue in existence. Each animal has its so-called enemy ready and at watch to deliver it from feebleness and disease; and the sudden destruction which awaits them all, without fearful premonition, and with little pain,—this killing in lieu of death,—instead of being, as it is sometimes regarded, a cruel feature in Nature's plan, is a happy provision for deliverance from the slower death which increasing failure or progressive disease would have involved, and which civilization entails."

So pleasing is the picture thus drawn that one is disposed at first to accept it as correct in every detail; but a consideration of the hard facts of pathology shows that some modification of the conclusions must be made. That there must be a well-ordered and regulated decline in the several organs, in order safely to pass the period which succeeds maturity and before old age is attained, is a just statement of an important fact, and at this stage there is nothing discoverable in the tissues which our present methods of pathological investigation give us the right to call disease, although our knowledge of the

changes which occur later makes it highly probable that they had started early during the period of decline, at first remaining indistinguishable. As the description is continued the word decay is used, and it is called physiological decay. In later portions of his work Humphrey describes the changes in the body attendant upon old age, —the alterations in the bones, the enlargement of some organs, and the shrinking of other parts. Although the idea of a physiological death would be very fascinating, with the hope that the time will come when human beings shall escape from the world without having to suffer the humiliations of sickness and the pains of disease, yet such an end seems hardly likely, for that which has been described as physiological decay is identical in its pathological lesions with what has been called Bright's disease, or fibrosis, or, as I have ventured to call it, the *disease of age*.

CHAPTER III.

THE ORIGIN OF DISEASE.

One of the central ideas of all that has heretofore been said is that many diseases arise in consequence of latent changes which occur without producing external evidence of disturbance, and that therefore it is necessary to rearrange to some extent our views in regard to the origin of disease. This thought might be made to lead to the discussion of almost any subject connected with the causation of disease, but the effort will be made to restrict it closely to the central idea and to matters nearly connected.

A very important, probably the most important, secondary consideration is the fact that disease seldom confines itself to one organ. This fact is not usually given its just weight, and disease has been looked upon as due to inflammation or degeneration of one organ or another, without any consideration of changes in related parts and distant organs. A general survey of the whole bodily condition and study of the relations of the various parts one with another is absolutely essential to advance our understanding of the origin of disease. Cancer and sarcoma, which a few years ago were very generally confounded, and which even now are not always easy to differentiate, have probably been as much studied as any pathological conditions, and up to a certain point are well understood. Their appearances under many different circumstances have been carefully investigated, and so well are they known that it is often possible even to predict what will be their behavior in the future. When, however, we come to discuss their causes, it must be confessed that so far as concerns final knowledge we are as yet in absolute ignorance. The utmost that can at present be accomplished is to reason from the facts already collected in such direction as they appear to point. Formerly few considered malignant disease to be connected with any extrinsic cause, the general belief being that it arose from disordered action of the natural component parts of the body. At the present time, however, the world of medicine tends toward the theory that the origin of most disease is extrinsic; that there are material germs, either animal or vegetable in nature, and capable of growth and reproduction, which

are the causes of the great majority of diseases. Although no one ventures to assert that the causes of cancer and sarcoma are known, there is often a tone in medical writings which seems to indicate that those thinking upon the subject are convinced that there is an extrinsic cause, and that it remains only to discover it. In the mean time, however, we continue in entire darkness in regard to what the cause may be. Probably the most extraordinary feature of malignant disease, second to the fact of its existence, is the tendency to the production of what have been called secondary or metastatic deposits. Although no authorities assert that it is known that malignant disease is contagious or infectious, yet it seems to be almost universally accepted that there is something of the nature of infection which is operative in producing the metastases; that what is called the primary growth in some unknown way transfers a sufficient amount of the venom which is assumed to exist to distant parts and there reproduces itself. So far as concerns final knowledge of the cause of the metastatic process, we are no nearer to it than to an understanding of the origin of cancer and sarcoma, and the generally accepted assumption of the infectious origin of metastasis is only a convenient explanation of what in truth is as yet entirely beyond our comprehension.

A parallel may profitably be drawn between the malignant diseases cancer and sarcoma and the fibroid process. It has been mentioned in Chapter II. that fibrosis is the most striking and characteristic feature of age, and it was hinted that, as a result of disease, conditions and lesions almost identical with those inevitable in age are frequently to be found in youth, and even in infancy. Clinically it is found that when death has occurred from chronic disease which during life was ascertained to have attacked some one organ, fibrosis being the principal or an important lesion, the fibroid process is seldom confined to the organ in which it was known to exist. For example, in organic heart disease involving fibrosis of the muscle there may be an entire absence of symptoms of disease of other organs, and yet it can be confidently predicted that similar changes will be found to exist elsewhere. The same is true of contracted kidney, which is essentially a process of fibroid degeneration. Its companion lesions have been much studied and are well known. Fibroid disease of the heart, lungs, liver, and spleen, or of some of them, is an almost invariable accompaniment of contracted kidney. The fibroid changes in other places besides the kidneys are just as

much a part of this form of Bright's disease as metastatic deposits are of cancer and sarcoma, and are of just as frequent occurrence. The fact that fibroid degeneration, which constitutes the essential pathological change in many forms of chronic disease, is usually widespread is most striking and important. This characteristic of fibrosis will be more fully considered when the discussion and illustration of the pathology of the various organs are reached. Perhaps enough has now been said to illustrate the parallelism between the malignant diseases cancer and sarcoma, and fibroid degeneration. This parallelism consists in the fact that in the great majority of instances neither malignant disease nor fibroid degeneration is able to confine itself to a small district, but manifests a tendency to spread over a large extent of territory in the organism in which it has once established itself. In regard to malignant disease it is commonly believed, and often assumed as established, that its spreading is the result of infection, of the transfer of a venom from place to place. On the other hand, if it were asserted that there is anything infectious in the nature of contracted kidney or of fibroid degeneration of the heart, such an idea would only excite ridicule. Cancer is the result of riotous growth of epithelium and fibrous tissue; in soft cancers the epithelium preponderates, and in the hard varieties the amount of fibrous material is greatest. The growth takes place at the expense of the natural elements, which are compressed and pushed aside or destroyed. Sarcoma is a similar process, but mesoblastic tissue plays the part that is taken by epithelium in cancer. Fibrosis consists in an unnatural and unhealthy growth of fibrous tissue, and it also takes place at the expense of the natural constituents, which are thrust aside or destroyed just as in malignant disease. Morbid fibrosis is of slower progress than malignant disease, and the morbid fibroid material is prone to inflammation. It is to the combination of latent fibroid growth with inflammation, mingled in every possible way, that is due the greatest part of the chronic disease of old age and middle life, and even of the young who are prematurely aged. The tendency to destructive suppuration is a trait common both to malignant disease and to fibroid degeneration. Should it be possible for any one to suppose, after reading the foregoing, that it has been my intention to indicate a belief that Bright's disease, cardiac fibrosis, or other similar condition can, under any circumstances, have an infectious element, my underlying thoughts have not been clearly suggested. Further, if it has not been indicated that there is absolutely no existing evidence supporting

the widely prevalent belief that the metastasis of cancer and sarcoma is due to a process of infection, my expression has lacked clearness. To sum the matter up briefly, the result of a careful review of the facts that have been ascertained is to make it patent that the two malignant diseases and fibroid degeneration present many points of parallelism, especially the remarkable tendency that both exhibit to spread. The spreading of the two seems so similar that it is hard to escape from the conviction that the reason is the same in both instances. It may be asserted without fear of contradiction that the spreading of fibroid degeneration has nothing of the nature of an infection. If it were conceded that malignant disease and fibroid degeneration spread as they do owing to similar causes, and that the spreading of fibroid degeneration is not the result of infection, it would follow as a necessary corollary that the metastasis of malignant disease cannot be of the nature of an infection.

Before turning from the subject of malignant disease, it may be well to mention one or two curious facts bearing upon what has been said. Sarcoma is not rare in youth, while cancer is a disease of middle life and of the aged. Sarcoma is very like inflammation, and often it is impossible to distinguish by the appearance alone a sarcomatous deposit from inflamed or granulation tissue. No one who has paid close attention to the subject can have failed to notice how often, in studying cancerous tissues with the microscope, there are found also extensive disease of the blood-vessels and general fibroid degeneration. It may, of course, be said that this is only what should be expected, as cancer is a disease of advanced life, and it has been shown that fibroid change and vascular disease are essential features of age. The association, however, of fibrosis and arterial disease with cancer is of such very frequent occurrence that, although it would be easy to dismiss it as only coincidence, it is impossible to avoid the thought that the fibroid process, by its effect upon the blood-vessels, and thus upon the circulation, may have some predisposing or even causative relation to cancer. A singular condition, and one that supports the belief that cancer is only the result of ill-ordered growth of natural constituent parts, is that it sometimes happens that there is found, in persons who have died of other diseases and who are evidently not cancerous, a growth having all the characteristics of malignant neoplasms. Such a growth is illustrated and described in the chapter on the kidney (page 143). The clinical history and results of the post-mortem examination in this case forbid the belief that the growth

could have been an ordinary cancer. The microscopical appearance of small sarcomatous growths is less characteristic than that of cancers; the contrast between the neoplasm and the natural tissues sometimes, and between it and inflamed tissues always, is much less sharp. It has happened to me again and again to find, in the fat layer covering inflamed hearts, and in tubercular lungs, deposits of round cells presenting all the objective characteristics of sarcoma.

The disease molluscum fibrosum, in which fibrous tumors, often to the number of hundreds, grow upon the surface of the body, is singular and impossible of explanation. In cases of this disease a tumor grows, and afterward others show themselves and the number increases rapidly. For two or three years the tumors continue to increase in number and to grow in size. After an uncertain time, no new tumors appear, and the existing ones cease to grow larger. Such is very commonly the history of the disease. One cannot help perceiving the similarity in many respects between this disease and cancer. The multiplicity of growths in widely separated parts of the body is the same in both, and in molluscum fibrosum the tumors, both in their general characteristics and in their microscopical structure, are just as much heterogeneous products as are those of cancer. The strange attribute of cancer which is named malignancy consists solely in the fact that, once started, it inevitably progresses and increases until the life of the individual ceases. So far as can be seen, there is nothing specific or extraordinary in the manner in which cancer kills. Growth goes on until important surrounding parts are destroyed, the tumors themselves suppurate, or the person dies of exhaustion consequent upon the drain caused by the disease. The conditions in molluscum fibrosum are in every respect similar, except that the heterogeneous growths are confined to the surface of the body, and that, instead of inevitably increasing, they may cease to progress and remain as mere inconvenient obstructions. When cancer and sarcoma are divested of all romance and considered solely in the light of facts, they do not appear to be more mysterious than other pathological processes, and they are closely paralleled in many of their most essential peculiarities by various diseases, as has been mentioned.

Consumption is the scourge of the temperate climates, causing a greater mortality than any other disease, and, as the highest grades of civilization and intelligence have always existed in the temperate regions, its origin has been diligently sought. If the discussion could be confined to consumption of the lungs, for which phthisis pulmo-

nalis is an analogous term, it would be comparatively simple; but so soon as the word tuberculosis is introduced the matter becomes very complicated. No examination of the subject could be adequate without a consideration of tuberculosis, which, besides including almost everything that can be called pulmonary consumption, is made to cover many other conditions of disease which at different periods of the history of medicine have been variously classified. Perhaps some of the difficulties that have obstructed the progress of the medical observers and philosophers of the past may be avoided if two important principles that have already been mentioned are kept constantly in mind. These are, first, that disease seldom confines itself to any very restricted locality, and, second, that Nature has in disease followed her usual rule and drawn no abrupt lines, and consequently different diseases merge into one another so that it is often impossible to mark the line of separation.

In cases of pulmonary consumption it will be found that disease is seldom confined to the lungs, but that other and distant parts are generally involved. Consumption or tuberculosis is often intimately associated with conditions of disease that make it impossible to decide whether all the lesions are the widely spread results of a single process, or whether, on the other hand, the effect has been produced by separate diseases which have at the same time existed in one body. It is this that has caused the differences of opinion which have existed in regard to the unity or duality of the origin of consumption. The teachings of Niemeyer effected a most important advance in our knowledge of this strange disease, in regard both to its origin and to the possibilities of treatment. It would be impossible to give a more comprehensive exposition of his views, and of antecedent doctrines which he sought to confute, than can be obtained from his Lectures.* He opens as follows: "There is no subject in the whole range of pathology which more urgently requires a thorough reform than that of pulmonary consumption. In this field pathological anatomy is much in advance of clinical medicine. The term 'pulmonary tuberculosis' being still the one most commonly used for pulmonary consumption shows that the majority of the physicians and clinical teachers of the day abide by *Laënnec's* doctrine, and recognize but *one* form of pulmonary phthisis,—namely, tubercular phthisis. The dangerous tenets of *Laënnec's* doctrine, 'that pulmonary phthisis is a constitu-

* Clinical Lectures on Pulmonary Consumption, by Felix von Niemeyer; translated by C. Baeumler, The New Sydenham Society, London, 1870.

tional disease, that it never can develop itself out of acute or chronic pneumonia, or take its rise from a bronchial hæmorrhage, or from a neglected or protracted cold,' are up to this day taught in the medical schools as undisputed truths, and have in practice a most pernicious effect on the prevention and treatment of phthisis.

"*Laënnec's* dogma, that every form of pulmonary phthisis is caused by a specific new growth (une espèce particulière de production accidentelle), and that the cavities in the lung take their origin alone in the softening and the evacuation of this growth, was simply a *pathological hypothesis*, which, by the more recent researches in the field of pathological anatomy, has been entirely refuted."

This quotation indicates the opinion that consumption is not in all instances due to a specific new growth, but may arise in two different ways. It must always be kept in mind that Niemeyer uses the words consumption and phthisis as synonymous terms which describe the lung disease which has been so long known, but restricts tuberculosis to a much narrower field, allowing its application only to that form of phthisis which includes the deposit in the lung of the specific new growth which he calls miliary tubercle. In this view of the duality of origin lies the very pith of the doctrine of Niemeyer. He proceeds to endeavor to show that the two causes are inflammation of the respiratory apparatus and its termination in cheesy metamorphosis and destruction of the lung, and the development of tubercles, or, as it is more commonly called, tuberculosis. The tubercles are generally spoken of as miliary tubercles, and Niemeyer did not acknowledge the existence of any other form. He is decided in his expression of opinion that the large cheesy masses in the lungs which break down and form most of the cavities are not tubercular, but result from purely inflammatory processes. What Niemeyer meant by a miliary tubercle was not that which is indicated by the term at the present day,—namely, the minute bodies which develop in the meninges of the brain and spine, and in the coverings of the thoracic and abdominal organs and in the parietal layers of the pleura and of the peritoneum. It is strange that although he dwells so much upon the importance of miliary tubercles he nowhere distinctly defines them, the nearest approach to a description being the statement that they are gray and transparent.* Having endeavored to establish the duality of origin of consumption, Niemeyer divides the disease into three forms. The first form is that which is "brought about *alone by pneumonic*

* Loc. ci ., p. 2.

processes and their termination." Under this head he develops, with a lucidity and logic that are admirable, the opinion which has made him famous, that consumption is more often due to chronic catarrhal pneumonia than to any other one cause. The second form is that in which "tuberculosis has associated itself with the phthisis." It is striking that when Niemeyer came to make a classification of the disease for the use of clinicians he found it necessary to have the mixed form, the simple establishment of the duality of origin being insufficient for practical use. This is only another proof of the correctness of that which has already been so often reiterated, that Nature draws no abrupt lines and that diseases shade into one another. In connection with the second form of consumption Niemeyer expresses in the most decided manner the opinion that tubercles are generally a secondary product, and that tuberculosis is mostly secondary to the action of cheesy morbid products. At the same time he enunciates the dogma which has been more widely quoted than anything else from his writings, that "*the greatest danger to most phthisical patients is the development of tubercles.*" The third form is "primary tubercular phthisis." Niemeyer clearly declares his belief in the existence of primary tuberculosis as a specific new growth, and goes out of his way to refute the views of those who have stated that the doctrine of miliary tuberculosis is founded on errors. In reference to tuberculosis being of specific nature, in discussing the treatment, after insisting upon the curability of many cases of consumption, he adds the following: "Against that form of phthisis which consists in a *primary tuberculosis*, as well as against the *tuberculosis which has been developed in the course of phthisis*, treatment is indeed impotent." Niemeyer's lectures contain many other observations of great interest and value. He doubts if tuberculosis is inheritable, but believes in an "inherited disposition to pulmonary phthisis." He notes the frequency of phthisis in the emphysematous, and that an abundant formation of connective tissue takes place in the lung in consumption. This latter is a most important fact, and must be taken into consideration in any discussion of the disease. Congestion of the lungs, he says, is caused by excessive exertion of the body, and by direct irritation of the lungs and bronchi by foreign bodies, and such congestion may be the cause of phthisis. Niemeyer disapproves of the teaching of Buhl that phthisis is an infectious disease caused by the reception into the blood of the "tubercular poison," and comparable to pyæmia, small-pox, etc. Buhl's view he thinks is too exclusive and goes further than is war-

ranted by the facts. The keen discrimination and temperate wisdom of Niemeyer enabled him to note many important facts, but occasionally he is led into positions that are untenable. He teaches that hæmoptysis is a prolific cause of consumption, and says that the blood which is exuded into the air-sacs and bronchioles and not expectorated at the time of the hemorrhage causes pulmonary irritation and general febrile reaction, and, later, phthisis and even tuberculosis. The opinion of those who assert that hæmoptysis is due to the previous existence of latent tuberculosis he declares to be incorrect, and says that the hemorrhage is much more frequently bronchial, and that in such cases tuberculosis, if it arise at all, is secondary to the bleeding.

The weakness of this train of argument lies in the fact that there is no explanation for the hemorrhage other than the bare statement that it is bronchial. It is inconceivable that a bronchial hemorrhage could occur in a perfectly healthy person, and, as those subject to hæmoptysis in most instances have some form of consumption sooner or later, in the absence of any other explanation of the bleeding it is almost necessary to attribute it to the phthisical process. It is ungenerous to underestimate the importance of the work of our predecessors in the fields of science, and every one who considers the state of opinion before and after the enunciation of the doctrines of Niemeyer must acknowledge how great was the value of his contributions to our understanding of consumption. At the same time, however, that he firmly established certain facts, he failed to prove other things which he deemed equally fixed and important. The weakest point in his argument is his failure to draw clearly the lines of distinction between tubercular phthisis and phthisis resulting from inflammation. He gives no description which is adequate to enable others to recognize that which he calls miliary tubercle and says is a specific new growth and incurable. In failing to draw clearly this distinction, he failed to prove the central point toward which his whole argument was intended to lead,—the duality of origin of consumption.

The history of opinion in regard to the origin of consumption is most curious, and if we do not look back too far into the past it presents a strange series of oscillations. Laennec, who may be called the father of the modern views of consumption, believed it to be always the result of a single cause, a specific new growth, and, therefore, as incurable as cancer.

Niemeyer bestowed close attention upon the study of the clinical

history of phthisis, and, noticing how often it follows colds and acute disease of the lungs, read pathology in the light of these facts. His conclusion was that there must be a dual origin. His mind could not escape the conclusion which was forced upon it that inflammation of the air-passages and lungs causes consumption, nor could he decide to cast aside the doctrine, at that time accepted, that tubercle is a specific new growth; there was, therefore, no escape from the belief in two causes. The doctrine of Niemeyer of the duality of origin of consumption of the lungs was not accepted without dispute. For some time after its announcement there were many who refused to accept it, but gradually it forced its way, until finally it attained the position of an established belief. Next came the discovery by Koch of the bacillus tuberculosis. This was received by the world of medicine almost with acclaim. There was but little expression of opposition, and what there was was drowned by the general approval. It was soon considered as established that all cases of consumption of the lungs are caused by the presence and action of the bacillus. This, of course, overturned the structure so carefully raised by Niemeyer. It became impossible longer to believe in the duality of origin, and the teaching of Laennec that consumption is always due to one and the same cause, a specific new growth, became rehabilitated, but with this important difference: the source of the new growth had been discovered in the bacillus of Koch. At the present time throughout the civilized world it is generally accepted as true that consumption of the lungs is the result of a specific new growth which is caused by the bacillus tuberculosis. On the other hand, the inadequacy of any such doctrine to explain all the phenomena is so certain that the voice of opposition cannot be silenced, however popular may be the theory of an infectious cause.

From time to time statements are made and cases detailed which throw doubt upon the reasonableness of the belief that consumption of the lungs can be explained as always due to the one specific cause, the bacillus. As an instance in point may be mentioned the lectures of Clark,* in which the following statement is made: "It has been alleged by Koch—and is generally believed in London—that every case of phthisis, as I have defined it, is microbic, is associated with and dependent upon the presence and the action of tubercle bacilli. For my own part I presume to deny the allegation, and to contend

* Lectures on Cases of Fibroid Phthisis, by Sir Andrew Clark. The Lancet, July 2, 1892, vol. ii. p. 1.

that, whilst the great majority of cases of phthisis are bacillary, there is a considerable minority of cases which are non-bacillary, in which at no period of their history can bacilli be found. . . . Some years ago I had in my own wards three cases of what I designated as non-bacillary fibroid phthisis. I invited two or three of my more distinguished contemporaries to examine these cases, and to demonstrate the existence of the tubercle bacillus in them. They failed, and justifying their failure said, 'These are quite exceptional cases, and do not break down our generalization.'" Of course the statement of one man or the citation of a few cases cannot be considered to avail much to disprove a generalization such as that which has been built around the bacillus tuberculosis. The quotation from the lecture of Clark, therefore, is given not as proving the correctness of his contention, but simply because it is an example from an authoritative source of what always has been and what still continues to be asserted by many reliable clinicians. Their expression of view is of such weight that it is impossible to escape the conviction that there are cases of consumption, especially some of those of the more chronic form and usually classed as fibroid phthisis, that cannot possibly be due either to the bacillus or to any other infectious cause. This being the case, it is necessary to believe that they arise from some disordered action of the bodily organism itself, or, to be more precise, that they result from inflammatory action,—inflammation being given a broad definition, making it cover that which occurs in the tissues after a great variety of forms of injury. So soon as it is conceded that consumption ever is due to inflammation, the doctrine of the unity of origin which is associated with the bacillus of Koch falls to the ground, and we are forced back upon the two horns of a dilemma: we must either return to the teachings of Niemeyer of a dual origin or cast aside entirely the belief in the bacillus tuberculosis as the cause of consumption. So far as concerns human beings, there is no existing evidence, either clinical or experimental, which can, when judicially examined, be considered to show conclusively that consumption is infectious. With regard to experiments upon the lower animals, there have always been disputes among the experts in that field in regard to the conclusions to be drawn from tubercle inoculations. Moreover, it is not really known how far it is safe to make deductions in regard to disease in human beings from results obtained from experiments upon the lower animals. There cannot be any question of the existence of forms of consump-

tion which arise from inflammation, and, such being the case, it is much easier and more logical to look upon the bacillus as does Sutton,* who says, "It was looking for finer morbid changes that brought forth the bacillus investigation and revealed those feeders on the dead."

Before the time of the school of Laennec consumption was thought to result from inflammation, and even he was unable to escape the effects of that which he saw among his patients, for, after positively stating his belief that tuberculosis always has its origin in a specific new growth and is as incurable as cancer, he contradicts himself by saying he has known a few instances of recovery after tubercles had softened and caused the formation of cavities.† Niemeyer broke down this theory of unity of origin, and forced the acceptance again of the fact that colds and lung inflammations do cause consumption. The next swing of the pendulum resulted from Koch's discovery of the bacillus, which quickly brought into prominence again the belief in a single cause. Although this doctrine appeared to offer a resting-place for men's minds, which had been disturbed by the frequent changes of opinion in regard to the origin of consumption, and it was therefore received with favor, the voices of those who studied the disease at the bedside and in the post-mortem room were never quite silenced. Expressions of which the quotation from Clark may be taken as a type continued from time to time to appear, and when weighed collectively they prove conclusively the existence of an inflammatory origin of consumption. Since it has been proved that cases of consumption do result from inflammation, and since at the same time it has not been scientifically demonstrated that the bacillus tuberculosis ever is its cause in human beings, but only that the bacillus is present in the altered tissues of persons suffering with the disease, it is much more logical to believe that consumption is only the result of ill-ordered growth and disintegration of the natural component parts of the organism. To this conclusion my mind has been driven, after a prolonged and patient examination of such evidence bearing upon the subject as it has been possible to obtain.

Proceeding upon the basis that phthisis is not of specific origin or

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* Lectures on Pathology, by H. G. Sutton, p. 194.

† De l'Auscultation Médiate, par R. T. H. Laennec, Paris, 1819, tome premier, p. 60: "un assez grand nombre de faits me donnent la conviction intime que, dans quelques cas, rares à la vérité, un malade peut guérir après avoir eu dans les poumons des tubercules qui se sont ramollis et ont formé une cavité ulcéreuse."

of infectious nature, it is necessary to recollect that it often owes its origin to external conditions, but that these are quite different from infection. The influence of heredity is well explained by the sentence of Niemeyer, already quoted, that tuberculosis is not inheritable, but that there is an "inherited disposition to pulmonary phthisis." This expresses in simple language a truth well known to experienced physicians. The disease, however, frequently originates from external causes, which are much more tangible than so subtle a thing as an inherited trait. Neglected colds, chronic bronchitis, inflammation of the lungs, and pleurisy, often are the causes to start an attack of phthisis which ends only with the death of the individual. Diseases of the class named are caused by exposure to cold or other hardships, by any unhealthy mode of living which lowers the vitality, by dissipation, and by many other conditions.

Thus it is seen that consumption is, in its origin, different from cancer in that external conditions have a larger influence in producing it, but they are alike in that both arise without the introduction into the organism of any foreign substance as their primary cause.

Syphilis is a type of disease having a very different mode of origin. For its production direct contact is necessary with a material poison which exists only in some other individual who is at the time syphilitic. The poison is of a nature that precludes its transmission through the air, passing from one individual to another only by means of physical contact, or by inoculation, which amounts to the same thing. Thus the process is simple and easy to understand, but the disease possesses the characteristic that, once started, unlike most diseases of specific origin, which usually have a somewhat definite duration, it may run on for years, producing a train of symptoms and lesions which are well known to be syphilitic and which frequently end in death. Although the more remote tertiary lesions are as much a part of syphilis as the primary manifestations, the poison becomes with the lapse of time a less and less prominent feature, and in the later stages has disappeared. This statement is insusceptible of rigid proof, but there is every reason to believe it to be true that, for instance, tertiary syphilis of the nervous system cannot be directly transmitted. Some of the later lesions of syphilis cannot be distinguished except by the history from non-syphilitic cases of chronic disease. For instance, there is nothing in the appearances, either gross or microscopical, to render it possible to make a distinction between dis-

ease of the blood-vessels or of the nervous system due to syphilis and that which sometimes occurs in the blood-vessels and nervous system in the non-syphilitic. One of the most marked traits of the later stages of syphilis is its tendency to cause the production of morbid fibrous tissue. It is unnecessary to multiply examples, but as an instance of this may be mentioned the lesions of the liver which are ascribed to syphilis. These consist of scars principally composed of fibrous tissue which has grown in an organ that under natural conditions is almost wholly epithelial. The tissue of the nervous system, both the brain and the spinal cord, when altered by tertiary syphilis, becomes ordinarily harder than is natural, and any one who has studied the lesions carefully with the microscope will agree that, in association with other changes, the fibrous elements have greatly increased.

Syphilis, therefore, is a disease which in its origin is the opposite of cancer and consumption, for it can arise only in consequence of the introduction into the body of a specific material poison which there is reason to believe is of a nature heterogeneous from anything in the healthy tissues. It resembles cancer and consumption in that its more remote effect is a tendency to produce morbid fibrous tissue and many lesions that are identical with those common in various forms of chronic disease. A striking peculiarity is the waning strength of the poison and its final disappearance, although the effects of the disease may not only continue, but may actually become greater, so as finally to cause death.

Another class of disease is constituted by the ordinary contagious maladies, the poisonous principles of which pass from person to person through the air, without direct physical contact. It is not necessary to enumerate the diseases belonging to this class, the largest part of which is made up of the exanthemata, although there are others—as, for instance, whooping-cough and mumps—which are not characterized by any eruption upon the skin, and yet as certainly belong to the actively contagious diseases as do measles and small-pox. The origin of diseases of this class is entirely hidden from us, but their manifestations have been studied so that their usual behavior is well known. Although men's minds lead them to seek continually for material poisons as the sources of origin, still the search remains unrewarded. There is no reason why the poisonous principles may not be different from anything as yet known, for nothing has been discovered that affords any satisfactory indication in regard to their

nature. The actively contagious diseases, although their source of origin is still beyond comprehension, constitute as distinct a class as any one of those heretofore mentioned. At the same time, contagious diseases afford another example of the fact that nature draws no abrupt lines. There are diseases which are so near the border-line that clinicians continue to dispute whether they are contagious, and these are alternately placed in the contagious class or elsewhere, according to the oscillations of individual opinion.

The origin of disease is from two causes, extrinsic and intrinsic. There have now been mentioned four great divisions of disease, typified by cancer, consumption, syphilis, and the ordinary contagious diseases, such as measles. The first two are of intrinsic and the last two of extrinsic origin. Cancer is of purely intrinsic origin, arising solely from derangement in the working of the organism. The number of diseases belonging to the same class with cancer is very small. Consumption is also of intrinsic origin, for it too arises from disordered action of the organism, inflammation playing the principal part in its production. It differs from cancer in that external surroundings have often a large influence in its causation. Exposure, dissipation, hardship, or an accidental cold is often the starting-point of consumption. In some cases, however, in which the inherited tendency to phthisis is very strong, it is impossible to discover that any external influence has been at work. Such persons seem born to die of consumption, and no amount of care in the avoidance of possible external causes will prevent the growth in the lungs of the solid masses, called tubercles, which become larger, and then soften, causing death despite every precaution. Cases of phthisis of this variety are very like cancer in their mode of origin, as they are the result of ill-directed growth and destruction of natural tissues for which no cause as yet appears. The number of diseases that must be classed with consumption is immense, including almost all those of chronic form and all those due to atmospheric influences and other unhealthy conditions of the surroundings and mode of living of human beings. Syphilis is of purely extrinsic origin, and its poison is transmitted by physical contact only, being incapable of passing through the air. It stands entirely by itself, there being no other disease of exactly similar nature. Its most striking peculiarities are that the poison disappears during the later periods, and that the lesions it produces are in many respects identical with those of chronic inflammatory diseases.

The contagious diseases so evidently constitute a class by themselves that it is unnecessary to say anything more to demonstrate this fact.

With some one of the four types named all known diseases can be classed. The condition is the usual one in science: the principle is easy to recognize, but its application is difficult. The division of diseases into four classes is sufficiently broad and elastic to receive them all, but it is often difficult, sometimes impossible, to know where to place individual forms. In some cases it cannot be decided whether a particular disease is of extrinsic or of intrinsic origin. Dysentery, for instance, is often epidemic, and yet it has never been shown to be truly contagious, or even that there is any extrinsic cause, and it seems likely that it is due to climatic conditions and the general surroundings and food. The difficulty, therefore, in classifying the disease is that it is not sufficiently understood to enable us to place it. Is it truly contagious and like measles and small-pox, or is it simply the result of inflammatory destruction of the mucous membrane of the intestine, and of like nature with the phthisis which follows chronic catarrhal pneumonia as described by Niemeyer? Typhoid fever is at present generally regarded as a specific disease, and most of those even who do not believe that the germ which causes it is yet known are satisfied that there is a single specific cause, and that sooner or later it must be discovered. It is not many years since Murchison, after studying and tabulating several thousand cases, expressed the opinion that typhoid (enteric) fever may arise *de novo* under circumstances where the conditions necessary to its production exist. Since this conclusion was enunciated, absolutely nothing has been discovered in regard to the origin of typhoid fever which a logically scientific mind can accept as proof that the disease is specific. Here again is met the difficulty of classification on account of the lack of understanding of the disease. Diphtheria is another disease that has never been permanently placed, because its mode of origin is not known, although most persons at the present time believe it to be caused by a bacillus. Clinical investigation shows that it is in many respects dissimilar from the actively contagious diseases. Diphtheria, typhoid fever, and scarlet fever present a number of points of similarity. They are not so contagious as some other diseases, and they take possession of a locality and attack persons who live within the infected region in a manner that has no parallel in the behavior of the ordinary contagious diseases. This subject has been discussed by me in an essay

published some years ago.* Many facts seem to indicate that diseases such as the three named can, when the conditions necessary to their production are brought together, arise *de novo;* that they are capable of something very nearly like spontaneous generation, but that, once started, their existence may be continued by contagion. A sufficient number of instances has been brought forward to indicate that classification of disease is difficult, because it is as yet impossible to have any adequate understanding of many diseases.

No question can be of greater importance to the practical physician than that of the origin of disease, for so soon as the origin is known the most important step toward conclusive diagnosis has been taken. It is generally easy to ascertain where the original cause produces its first effects, and thence to follow the more remote results until, as often happens, the process becomes a very complicated one. The diagnosis being certain, a satisfactory prognosis can generally be made, and it is seldom difficult to decide upon the proper course of treatment.

The class of diseases in regard to which our understanding has most greatly advanced in the last century is that which owes its origin to the passage of time and to the environment of man, these being the ordinary inflammatory and chronic diseases. In regard to cancer and small-pox, which represent two different types of disease, nothing new has been learned except the little acquired by the study of the microscopical changes which occur in the tissues. Much the same may be said of syphilis. The inflammatory and chronic diseases cause an immense proportion of the total bulk of the suffering and disability and of the deaths of human beings. At the present time there is a tendency to regard diseases as belonging to one organ or another, and for this reason to take a narrow view. To obtain a comprehensive grasp it is necessary to consider the general bodily condition, and it is of the highest importance to remember that disease does not usually confine itself to a restricted territory, and that most chronic and inflammatory diseases are related, shading into one another in a way that is wonderful. The inevitable changes effected by the passage of time must not be overlooked, nor the fact that in man a bodily condition very similar to old age often results from his surroundings and mode of life, these being sometimes due to his folly or wilfulness, at other times to circumstances beyond his control.

* The Contagiousness of Scarlet Fever, by Arthur V. Meigs, The Medical Record, December 11, 1886, and The Transactions of the Philadelphia County Medical Society, 1886.

CHAPTER IV.

THE BLOOD-VESSELS.

ANATOMY is the foundation of medicine and pathology is an important branch of it. If one tries to utilize the facts of pathological anatomy in the management of disease, it at once becomes evident that pathology is also an important part of practical medicine. In dealing with this part of my subject it will be best to begin with a description of pathological conditions that have come under my notice. The observations were made in the wards of a general hospital, in which are treated many cases of chronic disease, but it will be necessary to include other facts such as commonly come under the notice of a physician. As all the tissues and organs of the body depend upon the blood-supply not alone for their healthy state, but even for their existence, it will be best to begin with a description of lesions of the blood-vessels.

Arteries.—The examination of a great many arteries has convinced me that if one seeks for histological arteries among those taken from diseased persons, such as ordinarily come to the post-mortem table, disappointment will be the result, for no man dies in health, unless killed by injury. In studying arteries, therefore, as they appear when examined with the unaided eye and when seen with the microscope, the pathologist is at once confronted with the difficulty of deciding what is normal and what appearances are to be considered the results of disease. The appearance of the tissues at an early embryological period is different from that immediately before birth, and a much greater difference exists between the tissues of an infant and those of an old man; but no distinct line can be drawn separating one of these periods from another, as each shades gradually into the next succeeding one. Little knowledge is required to distinguish an embryo from an octogenarian, but no degree of skill will enable an anatomist or a microscopist by examination of the tissues to decide the exact age of the individual from whom they were taken. Just as there cannot be found a dividing line separating youth from age, because the transition is gradual, so there is no sharp separation of health from disease. The microscopical examination of blood-vessels is more satisfactory in

its results than is that of organs, because there is no vessel in the human body so large but that a section of it at any particular point can be cut and examined in its entirety. Thus disease is more likely to be discovered, and a much better idea of the general condition is obtained than can be had of any one of the organs, from which, if the gross evidence of disease be absent, it is possible only to select hap-hazard a piece for microscopical examination. As not infrequently one portion of an organ is greatly diseased while the rest is healthy, it must often happen that important disease is overlooked.

Before proceeding to describe disease of arteries, it is necessary to give some account of their histological state, in order to make what will be said comprehensible. For convenience of description,* arteries are ordinarily divided into three classes,—small, medium, and large. The first includes the terminal branches, the second all the named arteries of the body except those like the aorta and the pulmonary artery, which are recognized as belonging to the third class. So far as concerns the adventitia and muscular coat nothing need be said, but the intima differs so greatly in arteries of different size that it is necessary to have an accurate conception of its ordinary histological conditions in order to recognize disease. In arteries of the largest size, of which the aorta is the type, the intima is thick and of complex structure, being composed, from within outward, first, of a layer of endothelium; second, of the subendothelial tissue, which consists of fibrous tissue, elastic net-works, and connective-tissue cells, and, third, of the fenestrated membrane of Henle. In medium-sized arteries the intima consists of endothelium, the subendothelial layer, which is composed of delicate fibrous connective tissue with branched corpuscles, and the internal elastic membrane, or, as it will usually be called in this work, the plicated membrane. The subendothelial tissue which separates the endothelium from the plicated membrane is absent in the smaller arterioles. In such arterioles, therefore, the intima consists simply of the plicated membrane and a single layer of endothelial cells. This anatomical fact it is very important to remember, for most of the arteries in the body are of this nature. Such arteries are too small to be seen to any advantage with the naked eye, and, as they are prepared and stained for examination with the microscope by the methods at present commonly used, the plicated membrane is very prominent and constitutes an important landmark to separate the

* Normal Histology, by George A. Piersol, M.D. Philadelphia, 1893.

intima from the muscular coat. In arteries of this size, therefore, any tissue lying inside the plicated membrane, except the single layer of flattened endothelial plates, may always be considered as the result of diseased growth. In terminal arterioles of the smallest size, in which the muscular coat has been reduced to a single layer of circularly placed muscle-cells, the intima consists of endothelium alone, there being no plicated membrane.

The commonest disease of arteries is thickening of the intima. A greater or less departure from the appearances which have been described as histological exists in a majority of the arteries which are examined by pathologists. Although from the stand-point of pure anatomy it is correct to say that every variation from the histological type is properly named disease, it becomes necessary for the physician to decide how great a departure from the normal standard must be present to be worthy of consideration. It happens that thickening of the intima is usually irregular in its distribution (see Figs. 4, 5, and 9), being often much greater upon one side of an artery than upon the other, or existing as irregular swellings variously placed. This irregular distribution of the thickening of the intima, together with the fact that in all arteries except those in the last stages of degeneration the plicated membrane is present to indicate precisely the separation of intima from muscularis, enables the pathologist to recognize with certainty the presence of disease. The great importance of changes in the intima will at once be recognized when it is remembered that its increase in thickness can take place only at the expense of the capacity of an artery to carry blood, which is the sole function of the arteries. Arteries answering exactly to the histological descriptions are seldom found post mortem, either in private practice or in hospitals. The intima usually is not a single row of flattened endothelial cells placed within the plicated membrane, but is a layer of connective-tissue material containing nuclei. In old subjects and in those who have suffered long with chronic disease the extent of this change in the arteries is commonly great, while in the young and in those whose health has been good there may be little or none of it. The lesser grades of thickening of the intima must therefore be looked upon as necessary accompaniments of advancing age in man, and as harmless so long as they remain slight. Their increase, however, is dangerous, for as the intima grows in thickness the amount of blood distributed to the tissue which the artery supplies is inevitably reduced. The thickness of the intima may be of any conceivable de-

gree, from the slightest proliferation of the endothelium at one portion of the circuit of an artery (Fig. 8, *c* and *d*) to total closure of the calibre (Figs. 3 and 13).

The muscular coat, although much less frequently diseased than the intima, is also liable to undergo change; it is often found to be irregularly thickened or degenerated, or even to be both thickened and degenerated (Figs. 4, 5, and 23). Variation in thickness of the muscularis around the circuit of an artery, if of sufficient degree to attract attention, is easily seen, and may always be positively asserted to be the result of disease, but it is more difficult to recognize slight degrees of degeneration.

The fibrous coat of arteries is, of the three layers, the least satisfactory to study, because it has no definite external boundary. The line of separation between muscularis and adventitia is easily determined with the microscope, but to fix the exact external boundary of the latter is impossible, for the adventitia is continuous with the perivascular connective tissue, with which it is identical in structure. It would have been better if histologists had assigned to arteries and veins only two coats, the intima and the muscularis, and had classified what is now named the adventitia or external fibrous coat as a part of the perivascular connective tissue. The truth of this observation is demonstrated by the examination of any section of tissue containing arteries or veins, for it is impossible to indicate a separation between the adventitia and the perivascular connective tissue. As the fibrous coat itself has no definite external boundary, it is evident that the study of its diseases is not easy, for it is impossible to decide whether changes outside the muscularis properly belong to the fibrous coat of the artery or to the perivascular connective tissue. The fibrous coat is much less frequently diseased than the muscularis, and still less than the intima. If it were acknowledged that the adventitia should not be classified as a part of the vascular system, but should be considered as belonging to the perivascular connective tissue, and as being thus only a part of the general connective-tissue system, it would make an important change in our manner of looking at disease. The whole of the great structure that has been built upon the doctrines originally enunciated by Gull and Sutton would have to be modified. Their view was that what they named arterio-capillary fibrosis had its origin in the external fibrous coat of arteries and in capillaries. If my view is correct, they were in error in supposing the condition to be one of truly vascular origin. No conclusive

FIG. 1.—OBLITERATIVE ENDARTERITIS (MODERATE THICKENING OF INTIMA). (× 20.)

From a woman of forty years who died of organic heart disease. The artery lies in the fat covering the heart. *i*, thickened intima; *p*, the plicated membrane; *m*, the muscularis; *a*, the adventitia; *x*, the pericardium; *y*, a nerve; *z*, the fat which covers the heart. In this instance the fat is normal in appearance.

FIG. 2.—OBLITERATIVE ENDARTERITIS (GREAT THICKENING OF INTIMA). (× 60.)

An artery from the wall of the Fallopian tube removed by operation on account of inflammation. *a* is the adventitia, which runs off into perivascular connective tissue; *m*, the muscularis, and *i*, the intima, which is so greatly thickened that only a small irregular calibre remains. The diseased intima, which is structurally connective tissue, is strikingly different in appearance from the muscular coat. The latter is of very uneven thickness and shades into the intima. No trace of the plicated membrane remains.

FIG. 3.—OBLITERATIVE ENDARTERITIS (COMPLETE CLOSURE OF THE VESSEL). (× 60.)

An arteriole in the fat covering the heart from a man of thirty years who died of organic heart disease. There is very little differentiation of coats. The muscularis is less closely knit together than natural, and is not easily definable from the tissue filling the calibre. This is a loose-meshed fibrous material containing a number of small openings. These openings are developing capillaries or cross-sections of cells of which the protoplasm failed to stain. The object depicted might be thought not to be a vessel at all, but for the fact that near it in the section there are others of similar appearance in various stages of closure.

Fig.1

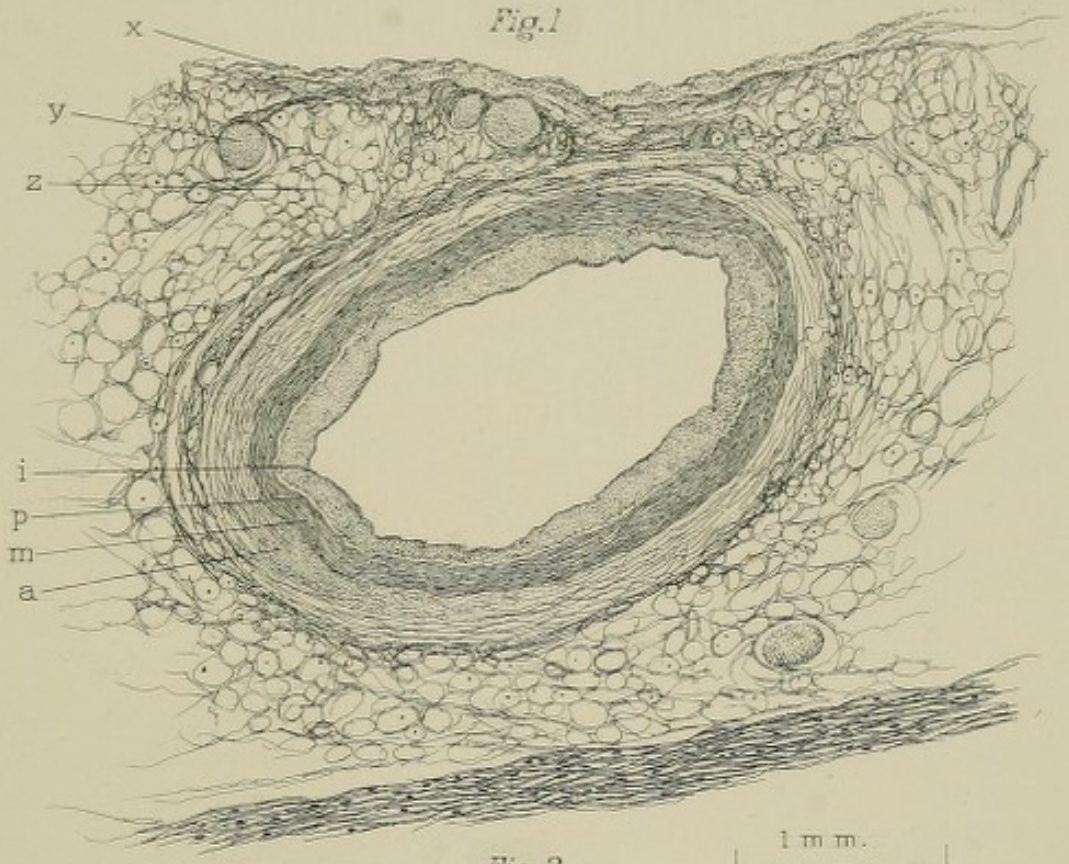


Fig.2

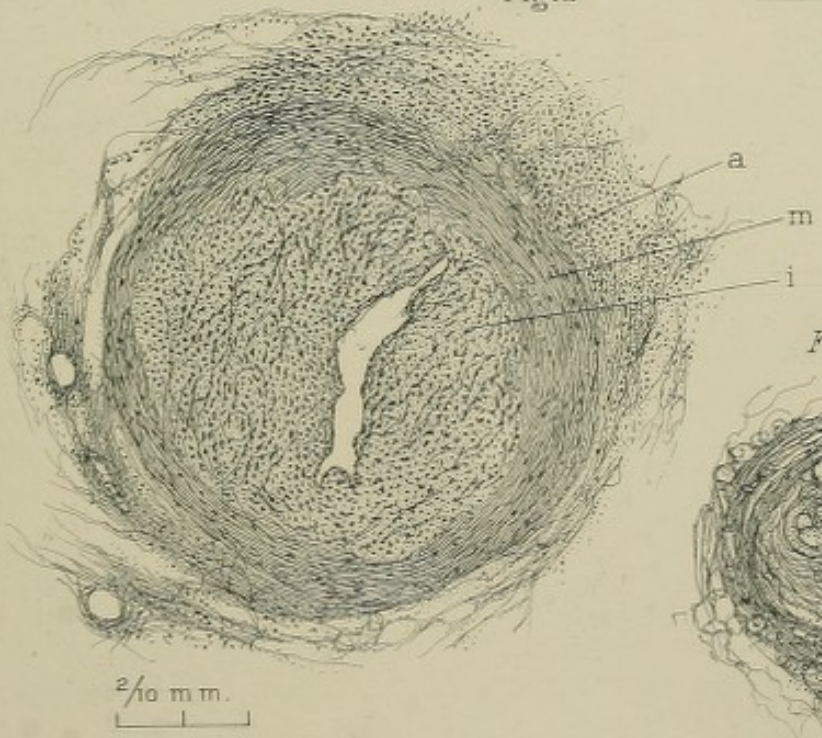
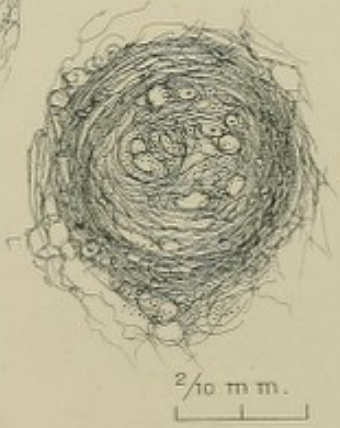


Fig.3



evidence has as yet been forthcoming to demonstrate the real starting-point of fibroid disease.

Various forms of arterial disease are illustrated by Figs. 1 to 17 inclusive. Figs. 1, 2, and 3 show three stages of obliterative endarteritis. Fig. 1 may be taken as a type of the commonest form of the disease. The artery lies in the fatty covering of the heart from a woman forty years old who died of organic heart disease with nutmeg liver and increase of fibroid tissue in the spleen and kidneys. In an artery of this size it might be expected, perhaps, that there would be some subendothelial tissue between the innermost layer of endothelial cells and the plicated membrane, but the intima is unevenly thick,—a condition under all circumstances unnatural,—and even at the point where it is thinnest it is at least four or five times thicker than natural. When examined with a higher power, such tissue may be at once recognized as pathological. The plicated membrane is very distinct, even with the low amplification used in making the drawing, and it marks a definite line of separation between the intima and the muscular coat. The muscular coat also is of uneven thickness, and such irregularity, whether of the intima or of the muscularis, is always to be considered an unnatural condition. The theory which attributes increase of thickness of the muscular walls of an artery to hypertrophy, and assumes that the vessel thereby acquires increased strength and greater efficiency of function, has no foundation in fact. Nothing is known from the clinical point of view to show that such an artery has greater muscular power than a healthy one with walls of natural thickness, and the theory rests solely upon the observation of the fact that the muscularis does increase in thickness.

Careful study with the microscope of such tissue has forced upon me the conclusion that the process is one of degeneration, instead of being reparative and compensatory. The amplification in Fig. 1 is not sufficient to exhibit the histological composition of the muscular tissue, but in Figs. 5 and 23, as well as in others of the series of illustrations, it is plain that the muscular tissue is greatly degenerated and weakened. The fibrous coat (Fig. 1) presents no positive evidence of disease, although probably there is slight inflammatory infiltration in places. It demonstrates, however, very well the correctness of the statement already made, that there exists no landmark by which to fix the external boundary of the adventitia. Is all the fibrous material between the muscularis and fat adventitia, or is part of it perivascular connective tissue? And where is the line of separation? In Fig. 2

is exhibited a more advanced stage of obliterative endarteritis. The artery is from the wall of a Fallopian tube removed by operation on account of inflammatory disease. Cell-proliferation was excessive; the calibre of the vessel is a mere slit, and the intima is of enormous thickness. The structure of the intima is that of a rapidly growing fibrous connective tissue, and in this instance there is not the slightest appearance of any vascularity. The muscularis is of such very different texture from the intima that it is easy to recognize the separation of the one from the other at all parts of the circuit, although there is no trace of the plicated membrane remaining. In arteries diseased to the extent of this one the plicated membrane has usually disappeared. The muscular coat is of very irregular thickness at different parts of the circuit. The adventitia in this case, as in Fig. 1, demonstrates the impossibility of giving it any fixity of boundaries, there being nothing to mark the separation of adventitia from perivascular connective tissue. Entire closure of a vessel is illustrated by Fig. 3. There is in it no distinct differentiation of the coats. The muscularis shades gradually into the intima, which has proliferated so as entirely to close the calibre. Although there is no central channel for the passage of blood, there are several small spaces toward the middle of the vessel. It is not possible in every instance to understand the nature of these apparent openings, but, so far as can at present be known, they are always either swollen spindle-cells cut transversely or capillaries cut across. This subject will be discussed in connection with Fig. 23, at page 52. The general appearance of the vessel (Fig. 3) is that of an irregularly growing connective tissue which had been subjected to the influence of inflammation. It might be asserted that the object is not a vessel, and with some show of reason, were it not that in the section there are others of somewhat similar appearance, in various stages of closure, which are certainly vessels. This artery lies in the fat-covering of the heart of a man thirty years old who died of organic heart disease. Important effects of obliterative endarteritis are exhibited by Figs. 4 and 5. These are two sections of the same artery cut less than a quarter of an inch apart. The calibre of the vessel has been so greatly reduced by endarterial growth that its capacity to carry blood is only a small fraction of what it was in health, but in addition the flow of blood was made more difficult by the irregular and changing shape of the tube through which it passed. As has already been stated, one of the striking peculiarities of the thickening of the inner coat of arteries is the

FIG. 4.—OBLITERATIVE ENDARTERITIS CAUSING DISTORTION OF THE CALIBRE OF THE VESSEL. (× 14.)

Artery from the heart of a man of thirty-two years who died of Bright's disease and heart disease. The fibrous and muscular coats and their points of separation are easily distinguished. The muscular coat is not of uniform thickness. The intima is enormously thickened, and irregularly so; it is eight times thicker on one side than on the other. On the side on which the intima is least thickened the plicated membrane can be seen forming a boundary between intima and muscularis. Opposite, where the intima is thickest, the plicated membrane is lost. The calibre of the vessel is irregularly half-moon-shaped instead of circular. Fig. 5 is another view of the same vessel.

FIG. 5.—OBLITERATIVE ENDARTERITIS CAUSING DISTORTION OF THE CALIBRE OF THE VESSEL. (× 14.)

Section of the same artery as Fig. 4, and cut less than a quarter of an inch from it. The thickening of the intima is very irregular, and the separation of intima from muscularis is in places lost. The plicated membrane has completely disappeared. The shape of the calibre in this view of the vessel is very different from its shape in Fig. 4: such sudden changes in the form of the column of blood within a short distance must interfere with the freedom of the circulation.

FIG. 4.

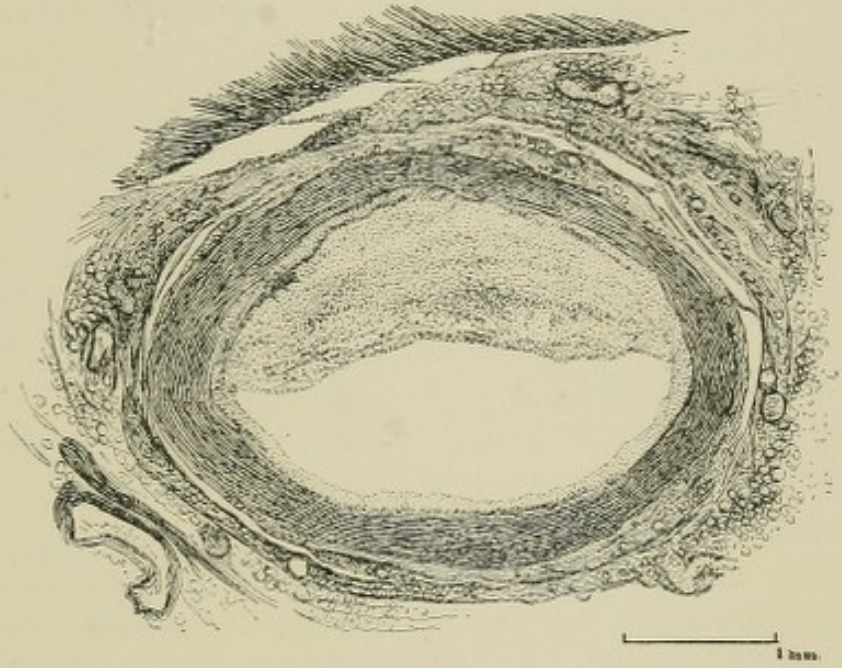
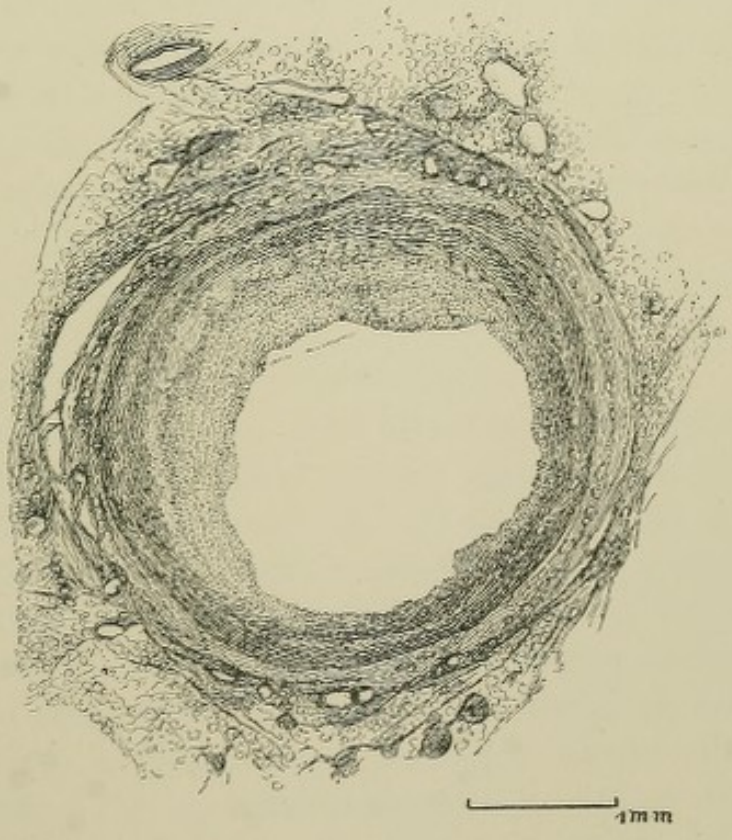


FIG. 5.



irregular and uneven method of its growth. The process of thickening is not governed by any known law, and the masses it forms are chaotic in their irregularity of distribution. The freedom of the current of blood through such a vessel as represented by Figs. 4 and 5 must be interfered with in at least two ways. It is well known that a circular tube carries a column of liquid with the least possible friction and the greatest rapidity, but in Fig. 4 the opening is irregularly half-moon-shaped, and in the acute angles not only would a fluid be checked in its course, but eddies flowing backward would arise. Besides, the shape of the opening in the vessel changes, for in Fig. 5, which, as has been stated, represents a portion of the artery distant less than a quarter of an inch from that represented by Fig. 4, the opening is nearly circular. The changing of the shape of the column of blood within so short a distance would necessarily cause retardation of the flow, as well as eddies. Besides the distortion and narrowing of the calibre of the vessel caused almost entirely by the growth of the intima, other interesting conditions of disease are illustrated by Figs. 4 and 5. In Fig. 4 the plicated membrane can be easily distinguished upon the side of the vessel where the intima is least thickened. In the drawing this has not been made so distinct as it should have been, and it does not show so well as when greater amplification is used. Upon the other side of the vessel it has been completely destroyed, and no trace of it is anywhere to be seen in Fig. 5. There is great degeneration of the tissue at the junction of the intima and muscularis in Fig. 5, and consequently the separation of them is less distinct than usual. In both drawings the muscularis is of uneven thickness, but the evidence of its involvement by disease is much more positive and greater in Fig. 5 than in Fig. 4. Consideration of the state of the adventitia, as usual, yields no certain results.

A condition of disease of great importance is shown by Fig. 6, which represents a longitudinal section of one of the main branches of the renal artery at its point of origin. It is from a man of fifty-eight years who died of Bright's disease, having greatly contracted kidneys. As usual in diseased arteries, it is the intima that has suffered most, it being thickened into irregular lumps which project into the calibre and obstruct it. Morbid fibrous tissue in its growth frequently produces an effect like that which results when a woman sews too rapidly: the material is puckered. When the intima becomes fibroid and lumpy near the branching of an artery, the likelihood of puckering is much greater than in any straight reach of the

tube. Such puckering as illustrated by Fig. 6 is of very common occurrence, and must be much more injurious than the same degree of narrowing at any other part of a vessel. The amount of blood to be distributed to the tissue supplied by such a vessel is greatly reduced at the fountain-head. When once a column of blood of a certain size propelled by a given force is in motion within an artery, its speed will be increased when driven through narrow places, according to well-known laws, but the conditions are very different when the entrance to a branch artery at its origin from the parent stem is narrowed. A liquid will flow in the direction of least resistance, and therefore, when the blood in passing along an artery reaches a branch narrowed or obstructed at the bifurcation, it flows on in the main stem, which is the direction of least resistance, sending but little into the obstructed branch, and thus starving the tissue to which it is distributed.

In studying disease of the heart it would be almost impossible to emphasize too greatly the importance of obstruction at the openings of the coronary arteries. There is no part of the human body more favorable to the development of the condition, and none in which it is of more frequent occurrence. The aorta, the largest artery in the body, and having thick walls, is more prone than any other to undergo atheromatous changes. The slightest thickening of its intima is liable to distort and narrow the entrances to the coronary arteries, and when once they are narrowed the current of blood must rush by in the great tube, leaving the heart itself to be starved. Fig. 6 demonstrates no gross changes of the muscularis or adventitia.

Fig. 7 illustrates an early stage of endarteritis. The artery is one from the anterior surface of the medulla oblongata of a man fifty-seven years old who died of Bright's disease. The changes are confined to the intima. The plicated membrane is many times thicker than natural, being in places equal to the muscularis, and it is opaque and contains many rounded cells of large size. Flattened endothelial cells are to be seen upon the inner edge. The appearances are precisely similar to those which are described as taking place in the cornea under the influence of inflammation, when it loses its transparency and becomes opaque and cellular. The appearance of this vessel lends further support to the statement already made, that it is a false classification which includes a fibrous coat as a part of an artery. In this instance there is nothing outside the muscular coat to call adventitia except the delicate pia mater, which here represents both fibrous coat and perivascular connective tissue.

FIG. 6.—AN ARTERY NARROWED AT ITS ORIGIN. (× 6.)

Branch of the renal artery from a man of fifty-eight years who died of Bright's disease. The vessel is cut longitudinally; from *h* to *h* is one wall of the main trunk; the arrow indicates the direction of the blood-current in the branch; *n* is placed in the narrow opening of the branch, which at *f* has its full width; *i*, *m*, and *a* are the intima, media, and adventitia respectively; *c* denotes points at which the intima is greatly thickened.

FIG. 7.—EARLY STAGE OF ENDARTERITIS. (× 240.)

An arteriole from the anterior surface of the medulla oblongata of a man fifty-seven years old who died of Bright's disease. The intima only is diseased. The whole of the light-colored tissue is the plicated membrane, which has grown so that in places it is as thick as the muscularis, and instead of being glassy it is muddy and contains many cells which are large and of rounded form. Flattened endothelial cells are still to be seen upon the inner edge. In a natural artery of this size the intima should consist of the clear, glassy, plicated membrane and a single layer of endothelial plates. The changes are similar to those occurring in the cornea, which becomes opaque and cellular under the influence of inflammation. The muscular coat presents no notable features, and the adventitia consists only of the fine fibrous threads of the pia mater in which the artery lies.

FIG. 6.

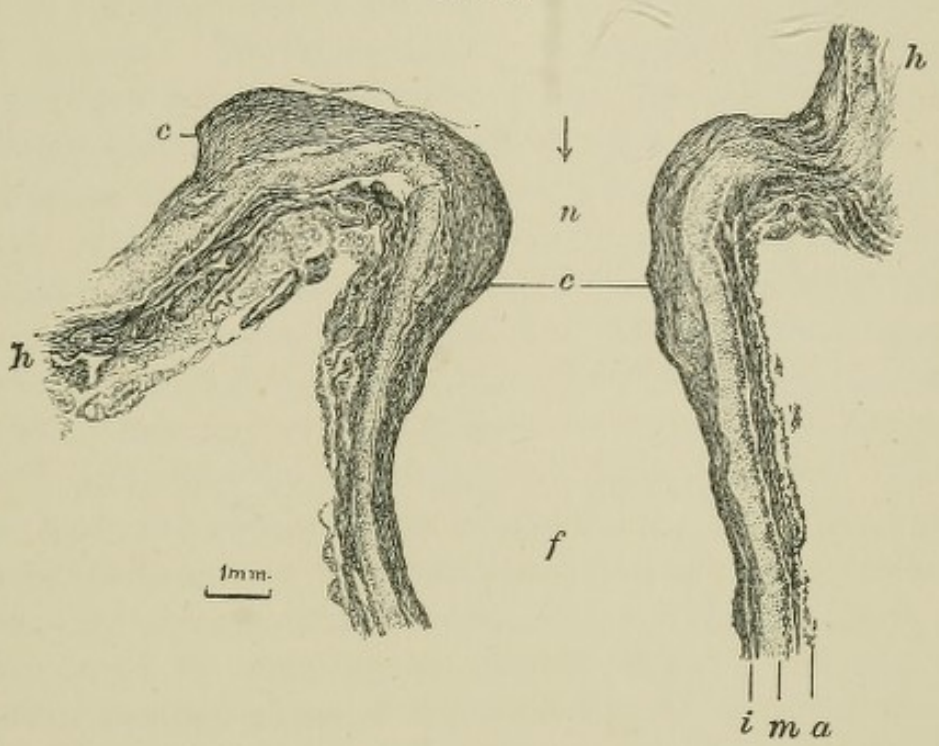
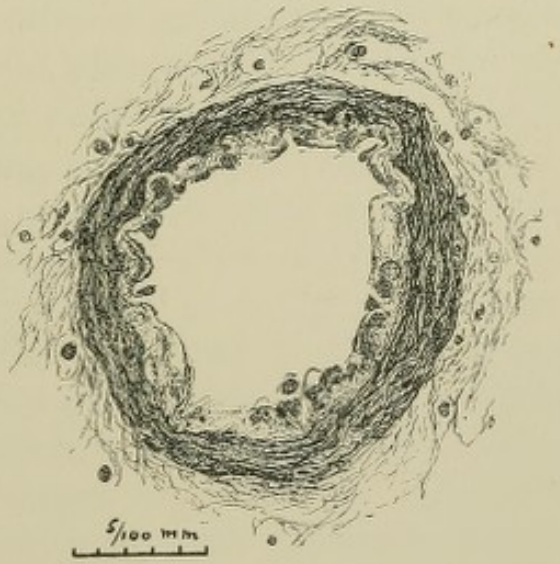


FIG. 7.



Figs. 8 and 9 illustrate two points in connection with disease of arteries: Fig. 8 shows the beginning of endarteritis, and Fig. 9 that the disease may exist fully developed at a very early period of life. The artery Fig. 8 is from the anterior surface of the heart of an infant six months old that died of wasting. The fibrous coat presents no points of interest. The muscularis is of slightly uneven thickness and its tissue is somewhat degenerated, but this can be satisfactorily demonstrated only by examination under higher amplification. The intima presents several histological conditions; at part of the circuit it is natural, and at other parts the plicated membrane has begun to lose its glassy, translucent appearance through infiltration of cells. As this opacity increases, the intima thickens until there is an area of considerable thickening, which histologically is fibrous connective tissue, and in this region the plicated membrane has disappeared, having been destroyed by the process of disease-growth. The illustration is especially instructive as it exhibits the mode of origin and progress of thickening of the intima as it comes on in an infant that died of wasting or marasmus,—a disease that produces effects similar to those induced by many of the chronic diseases of adults. Atheroma is but another phase of the same disease, many of the effects of which are produced only when the slow processes are changed for more rapid ones; but this is fully discussed elsewhere (page 54). That disease of arteries involving degeneration of the muscularis, destruction of the plicated membrane, and great thickening of the intima occurs in early infancy is fully proved by Fig. 9. This artery is from the anterior surface of the heart of an infant of five months that died of wasting, and it shows the disease in its full development. The intima is thickened around the entire circuit of the vessel, and there are two lumps which project into the calibre: in short, the degenerative process is precisely like that so common in the vessels of adults who have died of chronic disease. It is strange that disease of such a nature, which seems properly to belong to the aged, should also exist in very young infants who at the same time present many of the appearances of age. The caricature of age presented by a foundling infant with marasmus forms a picture too well known to require comment. Other methods of progress and effects of endarterial growth are shown by Figs. 10, 11, 14, and 15. Figs. 10 and 11 are two arteries of nearly the same size from a case of hydronephrosis, and they present interesting points of similarity and contrast. Both have enormously thick walls and reduced calibres,

but in Fig. 10 the muscularis has greatly increased, being at parts of the circuit much thicker than the intima. Again, one-third of the plicated membrane has been destroyed, while it is distinctly visible around the other two-thirds of the vessel. It is split in two at one place before it disappears. In Fig. 11 the plicated membrane is distinct around the entire artery and the muscularis is of uneven but very slightly increased thickness. The greater portion of the thick arterial wall is formed by the intima, which has grown to immense proportions. In neither artery does the adventitia present any notable features. These sections show well the structural difference between the diseased intima, which is a fibrous connective tissue, and the muscular coat, also how the plicated membrane divides the two, and when any portion of the plicated membrane has been destroyed, as seen in Fig. 10, how the one shades into the other. The most important lesson of all taught by the study of these two vessels, which are of the same size and were close together, is that, although they were subjected to precisely the same disease-influence, the effects produced were so different. The theory that disease of arteries commonly begins in the adventitia receives no support from such vessels as these, and, although the muscular coat is very thick in one of them, the appearance of the tissue itself is such as to foster the belief that the process is one of degeneration rather than of hypertrophy with an increase of functional power.

In Fig. 11 the muscularis is not greatly thicker than natural, while the increase of the intima has been enormous. Assuming, for the sake of argument, that the thickened muscularis of Fig. 10 had added strength corresponding to its increased bulk, is it conceivable that it could better have accomplished the function attributed to it, of contracting the calibre, while there lay such a mass of inert material within it as is constituted by the thickened intima? The appearances presented by the two sections go far to disprove the theory which is so generally accepted, that thickening of the muscularis which is common is a true hypertrophy. It is not an hypertrophy so far as concerns the arterioles, for the number of them I have examined is so great as to warrant me in making the assertion, but large arteries sometimes present appearances which might be thought to contradict it, although further examination of the subject will show that this is not the case. By large arteries are meant such as the radial, femoral, and renal, in all of which it is quite common to find the muscular coat greatly increased in thickness and the intima at the same time little beyond its

FIG. 8.—EARLIEST STAGE OF ENDARTERITIS, FROM AN INFANT. (× 90.)

An artery from the anterior surface of the heart from an infant six months old that died of wasting. *f*, adventitia running off into perivascular connective tissue, and *m*, muscularis; *a*, endothelium, and *b*, the normal plicated membrane, which has been thrown into folds by shrinkage. It appears as a translucent, glassy membrane, from which the endothelium has been slightly separated in course of preparation. At *c* is seen the earliest stage of disease. The plicated membrane is infiltrated with cells; to the right it is distinct, and to the left it disappears in growing cells. At *d* the process is further advanced, neither plicated membrane nor endothelium being distinguishable, their places having been taken by a layer of cellular material. At *e* the intima is quite thick, looking exactly as it so commonly does in older issues, and the muscular coat outside of it is thinner than elsewhere, probably because the intima grew partly at its expense.

FIG. 9.—ENDARTERITIS, FROM AN INFANT. (× 45.)

An artery from the anterior surface of the heart from an infant five months old that died of wasting. *f*, adventitia, and *m*, muscularis; *a* and *b* indicate greatly thickened portions of the intima, which is thickened around the entire circuit. At places the plicated membrane is distinguishable, and again it is lost; in the thickening (*b*) it has been entirely destroyed; it extends into *a* upon both sides, and is lost toward the middle.

FIG. 10.—OBLITERATIVE ENDARTERITIS. (× 55.)

From a case of hydronephrosis,—an artery from the kidney. The plicated membrane is a translucent, folded band, and is seen around two-thirds of the circuit. To the left, around the remaining third it has been destroyed, and the muscular coat and intima blend into each other in such a manner that there is no sharp boundary between them. In this region the muscular coat is much thickened and the intima relatively less so, the effect being that the muscular layer comes nearer to the calibre of the vessel than at other portions of the circuit in which the plicated membrane still persists. The plicated membrane, if followed from right to left above, is seen to split into two layers before it disappears. There is great thickening of all the coats; the muscular layer is irregularly thickened, and the thickening of the intima is immense, as it constitutes the largest part of the vessel-wall: it must be remembered that in the natural condition the intima of arteries of this size is only a thin layer of endothelial plates lying within the plicated membrane. (Compare with Fig. 11.)

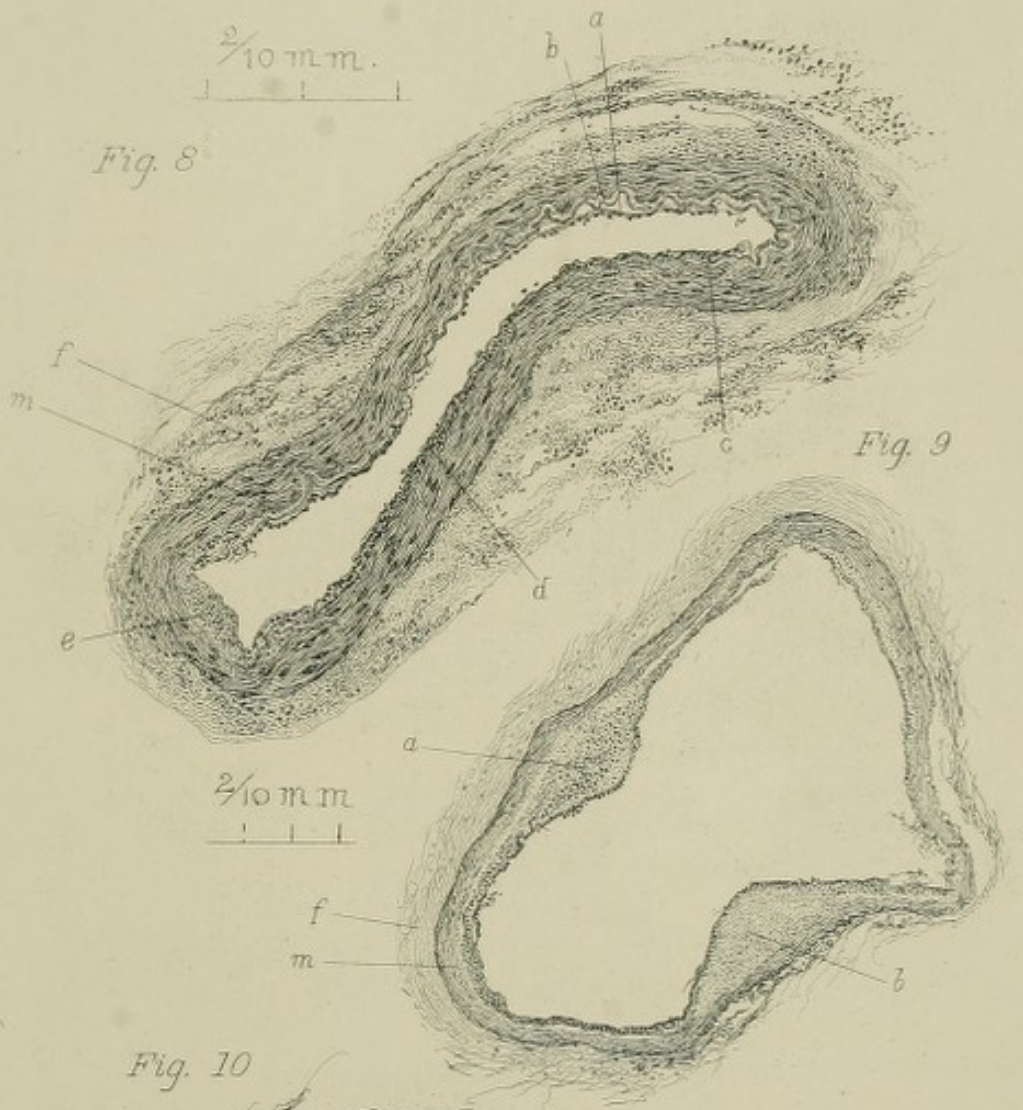


Fig. 8

Fig. 9

Fig. 10

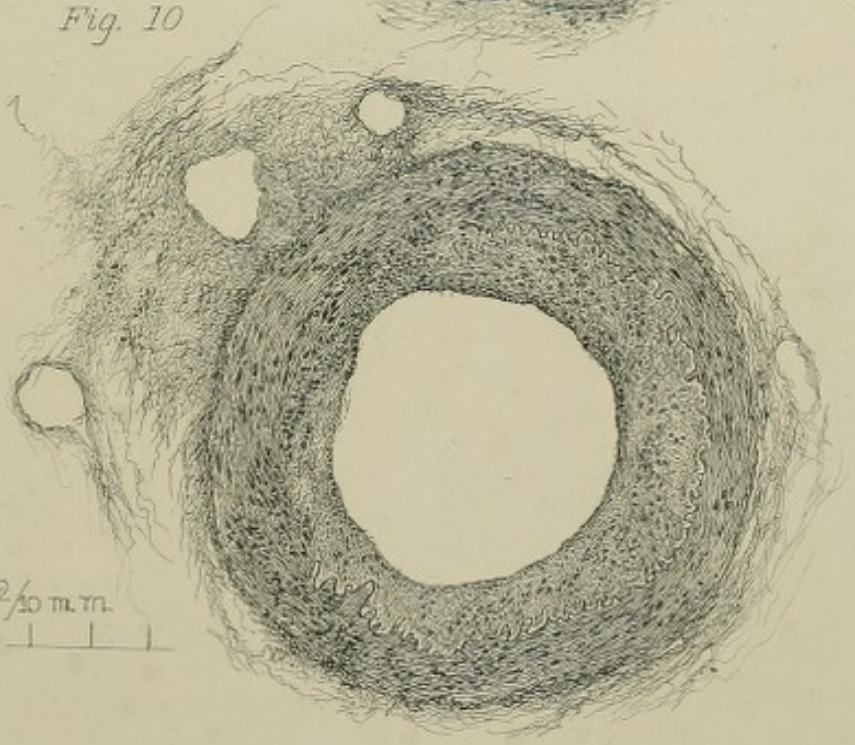
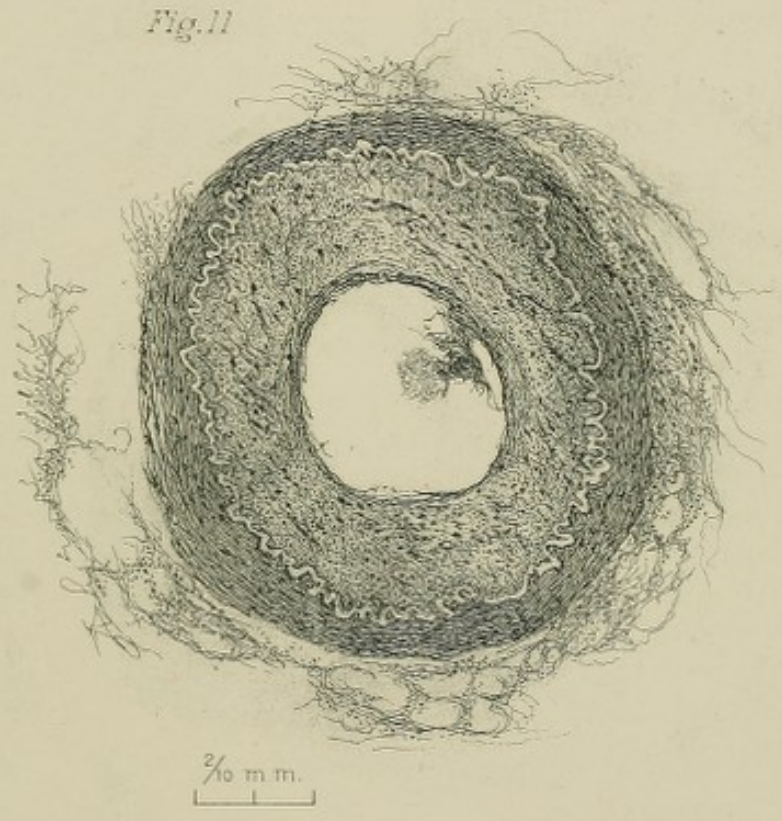


FIG. 11.—OBLITERATIVE ENDARTERITIS. (× 55.)

From the same section as Fig. 10: another artery. The calibre is greatly narrowed. The intima is enormously and irregularly thick, while the plicated membrane is most distinct around the entire circuit. The muscular coat cannot be said to be thicker than normal, but it is of irregular thickness, which is not natural. The two pictures demonstrate the irregular way in which the walls of arteries thicken so far as concerns the particular coat which shall take on increase: in the one the increase is almost entirely of the intima; in the other the muscular layer has suffered as much as or more than the intima.

Fig. 11

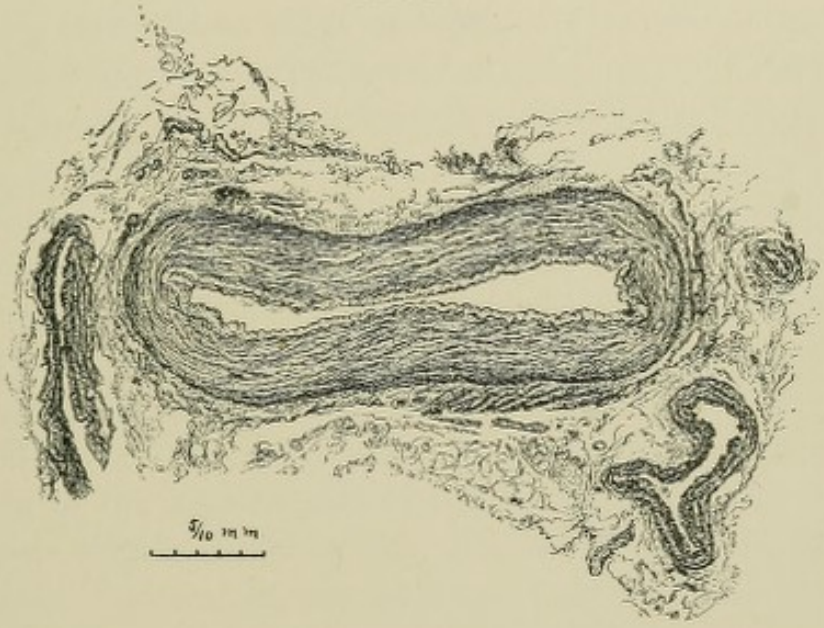


2/10 m m.

FIG. 12.—RADIAL ARTERY WITH THICKENED MUSCULARIS. (× 22.)

From a man thirty-one years old who died of Bright's disease. The intima is slightly and irregularly thickened, while the muscular coat is many times thicker than normal, and its tissue is degenerated. This degeneration of the muscularis is evident even with the low amplification used in making the drawing, but is much more so when the section is seen more highly magnified. The tissue is loose-meshed and open, instead of being closely knit as healthy involuntary muscle is. The intima is but little thickened while the muscularis is very much so,—which is an unusual form of disease of arteries. The muscularis is many times thicker than natural, and greatly diseased.

FIG. 12.



natural size. This fact I have adverted to in a paper published in 1888.*

The artery which seems most prone to take on disease in this form is the radial. Fig. 12 represents the radial artery of a man thirty-one years of age who died of Bright's disease. The intima is slightly thicker than natural, while the muscular coat is greatly increased. The appearance does not suggest that there is really an increase of the muscular tissue, although the condition is named hypertrophy of the muscularis. The muscularis, on the contrary, has degenerated into a loose-meshed and open structure, which contrasts strongly with the close-knit texture of healthy involuntary muscle. Arteries of large size are not considered to have much power to dilate and contract. Who supposes, for instance, that the circulation is ever influenced by contraction of the muscular coat of the aorta? The large arteries assist the current by their elasticity, which forces the column of blood onward during the intervals between the heart's contractions and helps to make even the flow. Questions of great interest arise in this connection regarding what is commonly called the high-tension pulse. High pressure within the arterial system is usually inferred from sphygmographic tracings and from digital examination of the radial pulse. In such cases the arterial walls are usually diseased, and, because the arterial wall is often diseased, the question should always be asked, What influence has the thickened arterial wall in the production of the high-tension character of the pulse?

Whatever degree of thickening may be found in the muscularis of large arteries, it is certain that in the smaller arterioles the commonest condition of disease is thickening of the intima. This occurs in all degrees, from the very slightest increase to total closure of the lumen; and, although the muscularis is also often involved, thickening of it alone without disease of the intima is of such rare occurrence that for practical purposes it may be said to have no existence.

Fig. 13 illustrates entire closure of an artery. It was taken from a negro man twenty-nine years of age who died of aneurism of the aorta. The vessel lay above the aneurismal sac, and was sufficiently near to be within the zone of inflammation induced by the growth; this accounts for its closure. An interesting feature is that so great an amount of disease could occur and yet there be no degeneration

* A Study of the Arteries and Veins in Bright's Disease, by Arthur V. Meigs, Transactions of the College of Physicians of Philadelphia, 1888; printed also in the Medical Record, New York, 1888.

of the tissue of the vessel at any part. The plug which fills the lumen is formed of a firm fibrous tissue, and in it are numerous rounded and elongated spaces. Study of these under greater amplification demonstrates that they are well-developed capillaries, and that the blood-supply of the new-formed tissue is quite rich. This cannot be determined from the drawing, because it is not sufficiently enlarged, but the openings can be seen. The plicated membrane is very distinct, and there is a second between the muscular coat and the adventitia. This outer plicated membrane, although described as sometimes present in arteries, is seldom so evident as in this instance. It is an unusual feature of the artery, for it very seldom happens that it is distinguishable.

By Fig. 14 is represented a peculiar condition of disease. The artery is from the kidney of a man of seventy who died of chronic myelitis and who had also contracted kidneys. In the sections of this kidney most of the arteries are diseased in much the same way as the one represented, and they present great variations in detail. Disease of the vessels is a necessary part of contracted kidney. The ordinary features of disease presented by the artery are thickening and degeneration of the walls and reduction of the calibre. It is not worth while to dwell further upon the fact that all forms of disease which induce thickening of the walls of an artery at the same time reduce its calibre. This artery, however, demonstrates a condition which is not shown by any of the other sections. The material forming the arterial walls has undergone so great a change that it no longer bears any resemblance to the tissues of which healthy arteries are composed. All differentiation of coats has disappeared, and the arterial wall is formed entirely of a loose-meshed, coarse, and stringy fibrous material poor in nuclei. At one spot in the thickest part of the wall is a small area in which the tissue is disintegrated and granular; this is probably a minute atheromatous abscess. It constitutes a type of an unusual form and degree of degeneration.

Fig. 17 represents a minute arteriole from the kidney of an old negro woman who died of general fibrosis, involving the heart, lungs, liver, spleen, and kidneys. The vessel shows endarteritis with great reduction of the lumen, and there is a small vessel in its wall which is unusual both in situation and in appearance. The tissue of the arteriole is so changed by disease and degeneration that but little trace of the usual component parts of a healthy vessel can be distinguished. The dark-colored material farthest from the centre is all

FIG. 13.—OBLITERATIVE ENDARTERITIS (COMPLETE CLOSURE OF THE VESSEL). (× 12.)

From a negro man of twenty-nine years who died of aneurism of the aorta: a small artery attached to the upper portion of the aneurism. *a*, adventitia, running off into perivascular connective tissue; *x*, an external plicated membrane sometimes seen in arteries, forming the boundary between the adventitia (*a*) and the muscular coat (*m*); *p*, the plicated membrane, within which the intima (*i*) has grown so that it entirely occludes the lumen of the vessel. This occluding intima is composed of a well-developed fibrous tissue, and contains numerous capillaries which show to some extent in the drawing as small spaces, but which can be well seen only when the preparation is examined with greater amplification.

FIG. 14.—OBLITERATIVE ENDARTERITIS. (× 120.)

An artery from the kidney of a man of seventy years who died of chronic myelitis and in whom the kidneys were contracted. The calibre of the vessel is very small and is eccentrically placed, and the walls are exceedingly thick. The appearance and structure of the tissue are unusual and peculiar; it is more nearly uniform than common, and resembles connective tissue poor in nuclei. It seems as if the muscular coat had grown, and in growing changed so as to lose all its ordinary characteristics. There is no trace of the thickened intima which is generally the most marked feature of endarteritis in small vessels. There are a few renal tubules and epithelial cells included in the picture.

FIG. 15.—DEVELOPING BLOOD-VESSELS. (× 120.)

From the same case as Fig. 13: a section of the wall of the aneurism. The drawing includes two adjacent vessels. *a*, the lumen of the upper one; it is eccentrically placed, and the opening is surrounded by misshapen endothelial cells; *b* is ill-developed muscular tissue. The walls are enormously thick, the calibre is nearly closed, and most of the tissue is like loose-meshed, rapidly growing connective tissue. The lower vessel has no opening. *c* indicates a region in which the lumen probably either had been or was to be developed. There is no appearance of differentiation of coats, either intima or muscularis, the tissue being composed of cellular material like connective tissue. The cells are arranged somewhat in whorls. It might be thought that neither of these growths is a vessel, but they were surrounded in the section by others whose appearance established the nature of the two depicted.

FIG. 16.—ARTERIOLE IN NEW GROWTH IN THE COLON. (× 240.)

A small arteriole from the thickened mucosa from a man of twenty-five years who died of dysentery caused by acute lead poisoning. Structurally the vessel bears no resemblance to ordinary arteries, veins, or capillaries, the tissue looking like epithelium. The mucous coat of the colon in the section from which the drawing was made is six millimetres thick.

Fig. 13

Fig. 15

Fig. 14

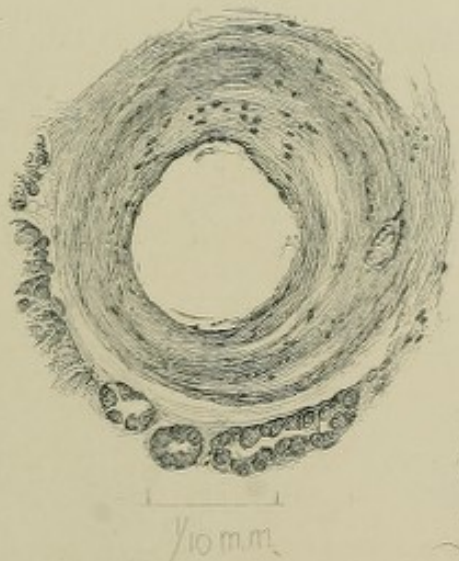


Fig. 16

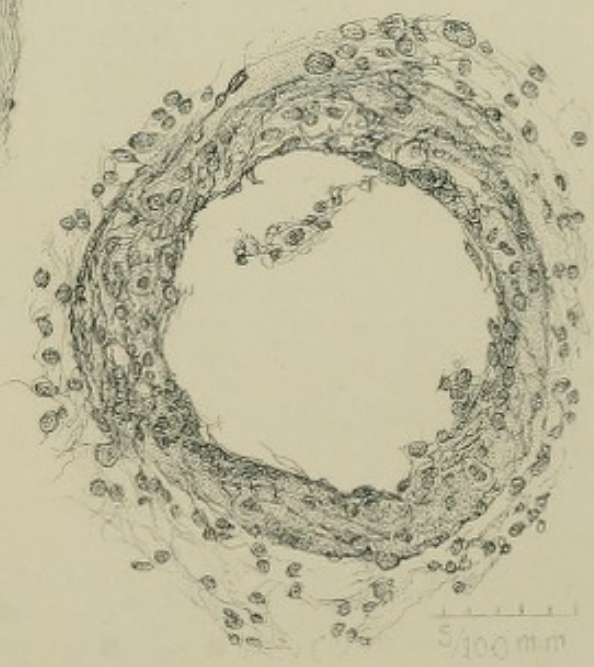
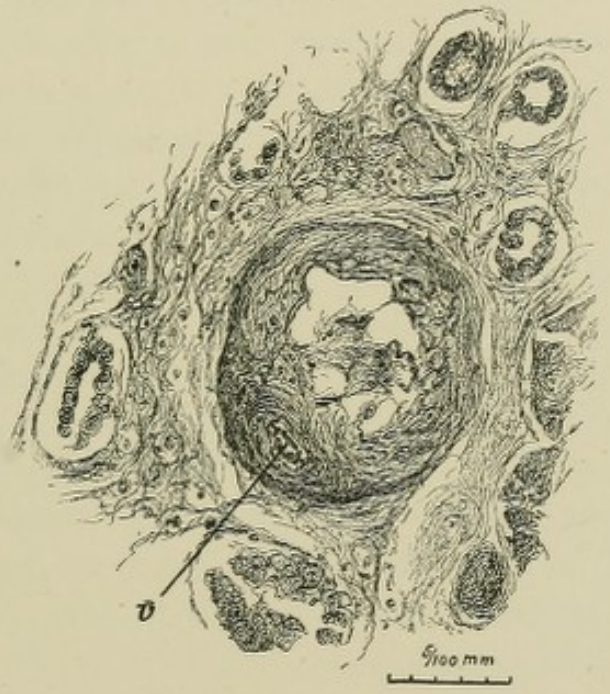


FIG. 17.—ENDARTERITIS AND A MINUTE VESSEL IN THE WALL OF THE ARTERIOLE. (× 220.)

From the kidney of a negro woman about seventy years of age who died of fibrosis involving the heart, lungs, liver, spleen, and kidneys. The lumen is almost closed by a cobweb-like mass of tissue, composed of nuclei and fibrous strings, which is attached to or forms a part of the vessel-wall. The wall is much thickened, and all distinct differentiation of coats is lost. *v* is a minute vessel in the wall.

FIG. 17.



that remains of the muscularis, while the loose, stringy, and richly nucleated connective-tissue material is the overgrown intima. In addition to the more solid portion of the intima adjacent to the remains of the muscular coat, there has grown a tissue in the centre which almost closes the lumen and looks like cobweb. This central growth may be taken as typical of one of the forms of endarterial growth that is sometimes seen in diseased vessels. The strings and shreds which extend irregularly across the opening of the vessel present a strange appearance. The blood-carrying capacity of the arteriole must have been almost *nil*. The minute vessel (*v*) in the wall might be thought to belong to the vasa vasorum, or to be a branch caught in the section so close to its point of origin that it had not yet escaped from the envelopment of its parent stem. It is almost certain, however, that it is a product of disease-growth, for in the natural condition a section of the branching of an arteriole never presents such an appearance; and it is still less likely to belong to the vasa vasorum, because such minute arterioles do not have nutrient vessels in their walls.

Among all the arteries which have thus far been described there is not one which shows disease of the fibrous coat, except thickening of the vasa vasorum, and, although in several the muscular coat is diseased, in no instance in which this is the case has the intima remained normal. On the other hand, in several there is disease of the intima without involvement of the other two coats. Most of the vessels depicted are from subjects who died of different chronic diseases, at ages varying from a few months to old age. The illustrations may therefore be considered as representative of the commonest forms of disease of the arteries.

It will be seen from what precedes that as a result of the common processes of endarteritis a great amount of new solid material is added to the organism in the form of tissue which grows within the arteries. New tissue is formed also in other ways, as, for instance, in the case of obliteration of the pericardial sac by pericarditis. This is not effected by a simple adhesion of the parietal and visceral layers of the pericardium, but a new tissue of greater or less thickness is formed between, and this new material binds the two layers together. A precisely parallel condition occurs in every case of adhesion of one organ to another or to surrounding structures: new material is formed between the opposing surfaces. The development of blood-vessels in the morbid tissue formed inside of arteries and in other

new tissues will be demonstrated; and it will be shown that, under the influence of disease, structures naturally avascular become vascular. It is well known that the adventitia of arteries and of veins is richly supplied with arterioles and capillaries which supply it with nutriment, and it is equally well known that these vessels do not penetrate the muscularis or the intima. The muscular coat and the intima therefore are in the natural condition avascular, and as they lie between the stream of blood and the richly vascular adventitia they must depend for their nutriment upon the soakage into them of blood from one or other of these two possible sources of supply. Which of the two is the main dependence is not certainly known, but it is generally supposed that the adventitia, which contains what are by common consent named the vasa vasorum, is principally instrumental in furnishing nourishment to all blood-vessels. It might perhaps better be said that this is assumed to be the case, for in truth there has been little evidence to decide the question. The growth of a great amount of solid material within an artery which has been shown to be one of the common results of endarteritis suggests the question, How is this tissue supplied with blood? Tubercles, being without blood-supply, are said to disintegrate as soon as they have grown too large to be any longer nourished by the soakage (osmosis) of blood into them. The case, however, is different with the new tissue in the walls of arteries, for, even when there is a great amount of it, as in Fig. 2, there is no necessary sequence of decay. The growth of vessels in the new tissue of arteries, in the new material formed by pericardial inflammation, and in other places naturally avascular is shown by Figs. 3 and 13 and 15 to 27 inclusive. It has been said (page 41) that some of the central spaces in Fig. 3 are to be regarded as vessels, and that the openings visible in the material filling the lumen of the artery (Fig. 13, page 46) are easily recognized as well-developed capillaries when the section is examined with higher amplification. Fig. 15 shows a pair of vessels in the wall of the sac of an aneurism of the aorta of a negro man twenty-nine years of age. They are from the same case as Fig. 13. Even if it be considered that the wall of the aneurism is but an enlargement of a natural tissue, being produced by the stretching of the aorta, it must be confessed that it is nearly the same as an entirely new tissue in this case, for the aneurism was an enormous sacculated one which grew out from the top of the aorta. It might well be thought that the vessels (Fig. 15) were mere irregular cellular growths, and not arte-

rioles, but in the tissue in which they lay they were surrounded by vessels of somewhat similar appearance, whose varying conditions establish positively the nature of the two selected for the drawing. The surrounding vessels were in various stages of growth, and were seen to have openings of different sizes, the appearances showing plainly that all belonged to the vascular system and were not mere ill-ordered cell-growths. The mode of growth is well shown: the cells tend to arrange themselves in circles or sections of circles which are more or less irregular. This tendency of cells to arrange themselves in whorls in young and rapidly growing tissues is well known to histologists, being a common appearance, for instance, in the skin of young organisms. That it frequently occurs as a result of pathological conditions is sure, for it is often seen in diseased tissue also, the most familiar example being the pearly bodies of skin cancer.

In the vessels under consideration there is no distinct differentiation of coats, although in the upper one there is material like ill-formed muscular tissue, and the minute opening, which is not centrally placed, is surrounded by cells resembling the endothelial lining of arterioles and capillaries. The main portion of both vessels is composed of a material which bears not the slightest resemblance to the tissues of which healthy blood-vessels are composed. It seems in some respects to resemble connective tissue, and again it is not unlike ill-developed epithelium. In the lower vessel there is no lumen, but one group of cells looks as if it was the one in which the calibre ought to have been developed, or in which it had previously existed and had been closed by disease. The picture presents a striking instance of exuberant and distorted cell-growth. The common appearances of the development of blood-vessels in embryos are well known, having been watched at all possible stages in the chick, which presents the best opportunity for their study, as well as in the human and many other embryos. The first stage of vessel-formation is the appearance of blood-islands; these are spaces with walls composed of a single layer of endothelium, containing embryonic blood-corpuscles. These so-called blood-islands would have been better named blood-ponds. When first formed they are separate one from another, but by their increase in length at either end they become joined to form tubes, which are the earliest capillaries. The walls of such of these tubes as are to form capillaries never increase in thickness, but are composed of endothelium alone. On the other hand, around such of them as are to be arteries and veins the muscular coat and the adventitia grow. In the

natural condition all newly developed blood-vessels have a distinct lumen, and their walls are composed of a single layer of endothelial cells; the wall subsequently thickens if the vessel is to grow large to become an artery or a vein. The growth represented by Fig. 15 presents an interesting problem, and one difficult, if not impossible, now to understand. The appearances presented by these vessels and by some of those next to be described forbid the belief that they had at any time large calibres and thin walls, as is natural. They must have been deformed from their very origin. Fig. 13 shows that, even in the adult, capillaries develop to nourish any new tissue that may grow in consequence of disease, and that such are in all respects like the normal capillaries. (See description of the plate.) Subsequent illustrations, described on page 53, show various stages of the process of vessel-formation. Besides this capacity of the organism to develop blood-vessels to nourish additions of tissue, another curious process of disease is illustrated by Fig. 15 and others of the series of drawings. There seems to be a natural tendency to produce blood-vessels in all tissues, diseased as well as healthy, but this conservative tendency is sometimes overcome. Fig. 15 shows in section two cylinders, one of which is quite solid and the other has only a small and ill-developed opening. It seems as if the formation of vessels had been prevented by riotous growth of cells, which has produced useless solid cords instead of tubes capable of performing the natural function of conducting blood. In the embryo, tubes are formed, as, for instance, the Müllerian duct in a part of its length, as solid cords of cells in which the opening is afterward channelled out, but this does not occur, so far as is known, in the case of blood-vessels. It seems unlikely, therefore, that such deformed vessels as these shown by Fig. 15 could later have opened to become useful vascular channels. Fig. 16 illustrates the production of a vessel in tissue naturally avascular when such tissue has greatly increased in bulk owing to the stimulus of inflammation. It is from the mucous coat of the colon of a man who died in the early stage of malignant dysentery induced by acute lead poisoning. The colon was enormously heavy and thickened. The mucous coat alone, after the tissue had been shrunk by being kept in alcohol as a preservative, was six millimetres thick, whereas the entire thickness of the healthy colon would not be one millimetre. The man died before sloughing of the mucosa had begun; whence the great weight and thickness of the intestine. It is hardly necessary to say that in the natural condition the mucous coat of the intestine has

FIG. 18.—ADHERENT PERICARDIUM AND COMPLETE OBLITERATION OF THE PERICARDIAL SAC, AND NEW BLOOD-VESSELS. (× 20.)

Section of the heart and its envelopes, from a child of ten years who died of heart disease. Above *a* is loose-meshed fibrous tissue; it lies upon the pleural side of the pericardium; *a* to *b* is the parietal pericardium; *c* is the visceral pericardium; *b* to *c* is new-formed tissue lying between the parietal and visceral layers of the pericardium. The new material contains many vessels (*v*), and these are cut in all possible directions. Between *c* and *d* is fat which usually covers the heart. At *c*, the surface of the heart, the fat is condensed and thickened, the oil-cells being smaller than elsewhere; *e* indicates vessels in the fat. The dark masses in the fat are strands of muscle. Below *d* is muscle, the wall of the ventricle. See also Figs. 19 and 20.

FIG. 18.

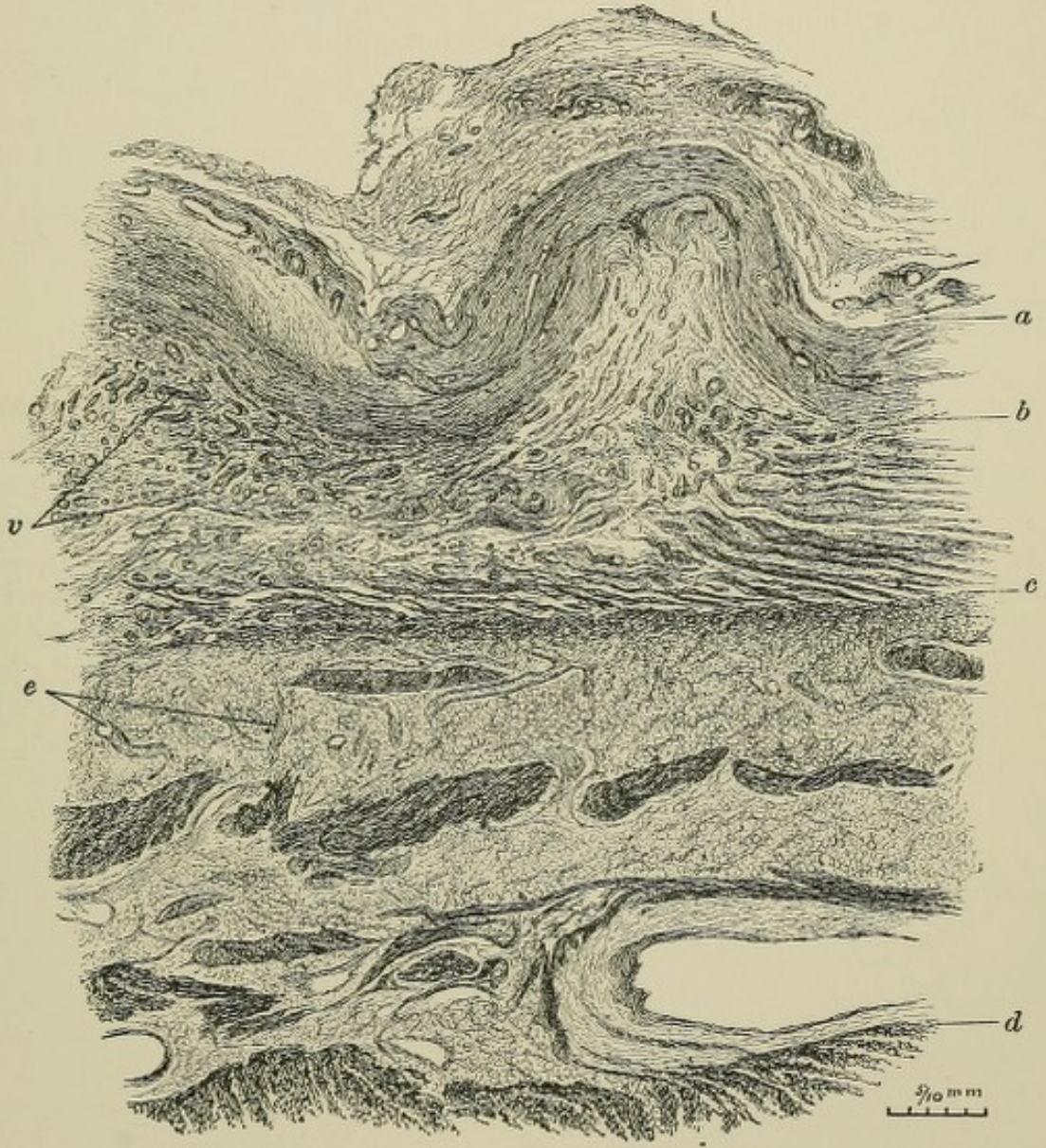


FIG. 19.—NEW BLOOD-VESSELS. (× 105.)

From the same section as Fig. 18 : a portion of the new-formed material between the two adherent layers of the pericardium. It is a loose-meshed tissue, containing many blood-vessels, which are curiously tortuous, so that they have been cut in all directions. The walls of most of the vessels are not very thick,—a little more so than ordinary capillaries, but not so thick as arteries,—and they are without any differentiation of coats. *a* and *b* are thicker-walled than the others, and both are cut transversely at their upper ends. At the upper end of *a* the opening is distinct and is ellipsoidal, while in *b* it is shadowy and seems as if closed by cellular growth. These two are represented more highly magnified in Fig. 20.

FIG. 19.

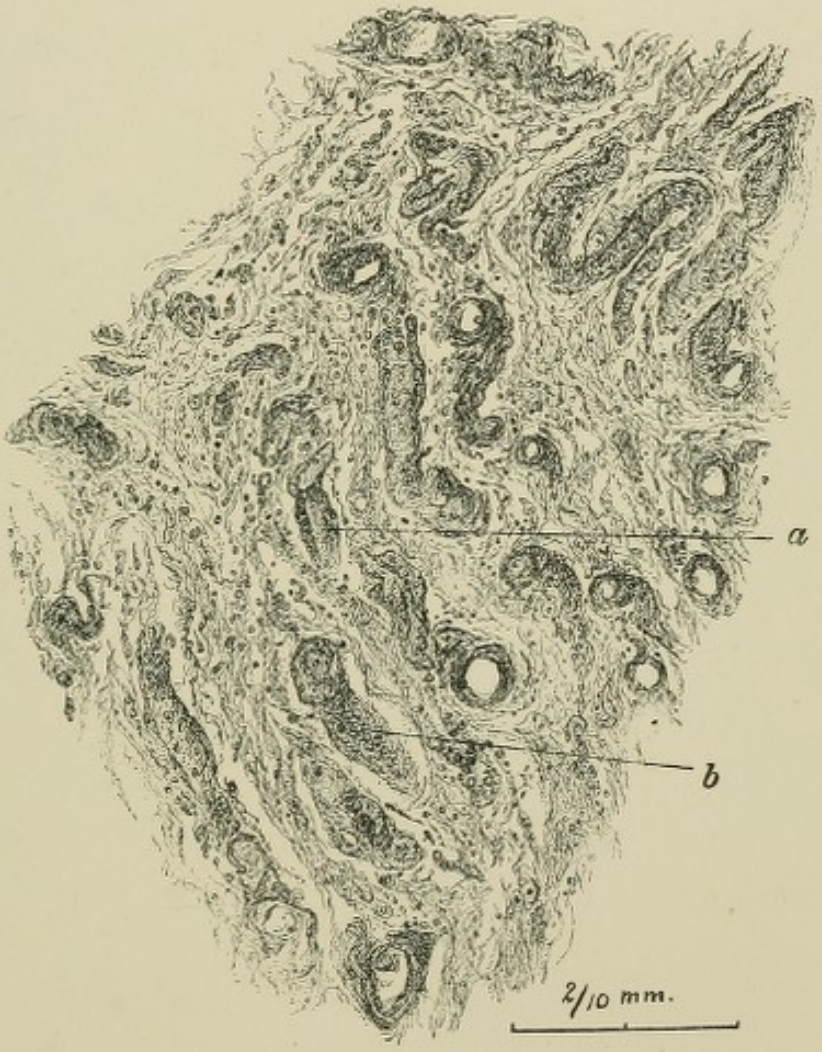


FIG. 20.—NEW BLOOD-VESSELS. (× 220.)

x is a more highly magnified view of *b*, Fig. 19; *y* is the same differently focussed; *z* is a more highly magnified view of *a*, Fig. 19; *x* was drawn with the microscope focussed upon the more superficial part. The end included between the two diverging lines from *c* is nearly circular, and within it is a smaller and ill-defined circle (*d*), which is the calibre of the blood-vessel plugged with cells. Below is the rest of the cylinder, and as here focussed to show its surface it appears to be composed of cells which are like epithelium. The whole lies in a lymph-space across which pass minute threads (*e*) of connective tissue which support and hold it in position; *y* is the same as *x*, but with the microscope focussed upon a deeper layer. The upper end is somewhat ill defined, while the lower appears as a capillary with distinct endothelial walls (*f*), and outside these walls upon either side is a thick layer of tissue containing cells like epithelium. The lymph-space with connective-tissue threads running across it is distinct in this view. *z* is *a* in Fig. 19, and in many respects it is like *x* and *y*. It is a developing vessel with thick walls which contain epithelial cells and is hung by fine threads in a lymph-space. The upper end of the capillary (*g*) is cut obliquely, and is therefore more elliptical than circular. Below at *h* the endothelial walls are seen where the capillary is cut lengthwise.

FIG. 20.

no blood-vessels in it so large as that depicted, although the rich capillary supply of the villi of the small intestine is well known. This vessel, therefore, which is to be classed as an arteriole rather than as a capillary, was developed owing to the conservative tendency of nature to give a blood-supply to all tissues which attain any considerable bulk. The vessel is peculiar not alone in the fact that it existed in the mucosa of the colon, but also in its structure and appearance. There is no sign of any differentiation into coats, although in a natural arteriole of such size the three coats would be easily distinguished; nor does the tissue of which it is composed bear the slightest resemblance to that of which the walls of healthy vessels are formed. It looks much more like epithelium.

Another phase of the development of vessels is shown by Figs. 18, 19, and 20. Fig. 18 represents a section of heart, including the two layers of adherent pericardium; these, with the new tissue between them and binding them together, are easily distinguished. Fig. 19 represents a portion of the new tissue more highly magnified, and it is seen to be like connective tissue in structure and to contain a great many blood-vessels. It is all a new development, the result of pericardial inflammation; its blood-vessels, therefore, are also new. They are numerous and tortuous, and many of them have natural-sized calibres. Some are so large that if they had been natural vessels they would have been classed as arterioles rather than as capillaries. Although they are of such a size as to render it just to look upon them as arterioles, and their walls are as thick as those of healthy arterioles, their structure is very different. There is nothing like the natural differentiation into coats, but the walls are composed of a somewhat ill-defined fibrous material. Among these vessels are two (*a* and *b*, Fig. 19) which are shown more highly magnified in Fig. 20. Their walls are very thick, and formed of tissue much more like epithelium than like that composing healthy vessels. It looks as if a thick wall had grown outside the endothelium. In some places the calibre appears to be closed. Altogether they present a type very aberrant from that of healthy blood-vessels (see description of figures), and they are in many respects like what is shown by Fig. 15. Figs. 18, 19, and 20, therefore, demonstrate three things,—the presence of vessels in new tissue, that these at the stage represented are structurally different from healthy ones of equal size, and that besides many capable of performing their functions there are many which are closed. Such closed vessels are probably the result of excessive and dis-

orderly cell-growth, a solid cylinder having been developed where a tube was needed. There is nothing which precludes the belief that new vessels in new tissue—such as most of those represented in Fig. 19—would in time have developed three coats and have become exactly like normal vessels of similar size and character.

The appearance of a blood-vessel developed in tissue naturally avascular is shown in Fig. 21. It is from the anterior flap of the mitral valve of a youth fourteen years old who died of organic heart disease. The valve was greatly thickened, and contained many vessels similar to the one figured. The opening of the vessel is very small, is eccentrically placed, and is bounded at a portion of its circuit by nucleated cells, which somewhat resemble those around the calibre of the vessel depicted in Fig. 15. There is no differentiation into coats, as in healthy vessels, and the tissue is of such unusual appearance that it is impossible to class it with any one of the healthy tissues; it has not the appearance of epithelium, of glandular, muscular, or connective tissue, nor of any of the healthy portions of the body. It is a loose-meshed material composed of fibrous threads and cells. The cells have large nuclei, around which is structureless material, and outside this is a fine ring, which is the external cell-wall. Again, there are cells which appear simply as rings enclosing structureless material (see description of figures). Fig. 22 represents cells similar to those shown by Fig. 21, but cut lengthwise and magnified twice as much. A portion of the tissue from which the section represented in Fig. 21 was obtained was cut perpendicularly to the first plane of section, and from this came the appearance represented in Fig. 22. The heavy edge shows the outer portion of a vessel (see description of figures), and the rest is made up of spindle-cells, most of which contain elongated nuclei. It is easy to understand why the cells in Fig. 21 appear as they do. The cell-body being composed of structureless material which remained unstained, it appears as an empty circle if cut above or below the nucleus, and as a nucleus surrounded by an empty space with the circular cell-wall around this if the nucleus be included in the section. Such peculiar cells are not rare in diseased tissues, and will be further discussed.

Figs. 23 to 27 inclusive represent the same arteriole cut at various levels; they show an unusual form of vascular disease and the development of blood-vessels in new morbid tissue. The vessel is from the lung of a girl twelve years old who died of organic heart disease. The first section cut was that from which Fig. 23 was drawn, and, the

FIG. 21.—DEVELOPING BLOOD-VESSEL IN A VALVE OF THE HEART. (× 300.)

A transverse section of a vessel of the thickened and diseased anterior leaflet of the mitral valve, from a youth of fourteen years who died of organic disease of the heart. The lumen is very small, is eccentrically placed, and around it are some nucleated cells (see Fig. 15). The vessel is almost a solid cord, and consists of loose-meshed tissue containing cells of peculiar appearance. *a* is a cell composed as follows: centrally a nucleus, around it a space which looks empty, and externally a distinct cell-wall. The empty appearance is probably due to rapid growth of the cell, or to the protoplasm's having absorbed liquid, or to its having contained colloid material which would not stain. Most of the cells are of the character of *a*; *b* is a cell cut across above or below the nucleus, and thus there appears only the cell-wall surrounding an empty space; *x* marks the boundary of the vessel, outside of which is the diseased fibrous tissue of the mitral valve. In the same section are to be seen numerous other vessels of this nature in various stages of development.

FIG. 22.—DEVELOPING BLOOD-VESSEL IN A VALVE OF THE HEART. (× 500.)

A longitudinal section of a similar vessel found in the tissue from which Fig. 21 was taken, more highly magnified. *a* is the outer boundary of the vessel (corresponding to *x* in Fig. 21); *b* is a spindle-shaped cell with an elongated nucleus and distinct cell-wall; it has the same appearance of emptiness as the cells in Fig. 21.

FIG. 23.—ENDARTERITIS WITH BLOOD-VESSELS IN THE NEW GROWTH. (× 300.)

Section of an artery from the lung of a child of twelve years who died of heart disease. *a* is the inner boundary of the vessel; *b* is the plicated membrane; *c*, an outer plicated membrane sometimes seen in arteries. Between *a* and *b* is the new growth, which consists of a loose cellular material. The cells are large, and many of them have large nuclei with spaces around them, and outside the spaces distinct cell-walls. In the new growth also are vessels (*v*); these have endothelial walls containing flattened nuclei and present exactly the appearance of ordinary capillaries. The plicated membrane (*b*) at parts of the circle is indistinct as a result of disease. Between *b* and *c* is the muscularis, which in places (*g*) has degenerated so as to be translucent and structureless. Outside of *c*, which is distinct throughout most of the circuit, is the adventitia running off into perivascular connective tissue. The shreds lying loose within the calibre are bits of tissue broken away from the lining, and other sections show them still attached: they dangled in the blood-stream.

Fig.22

Fig.21

Fig.23

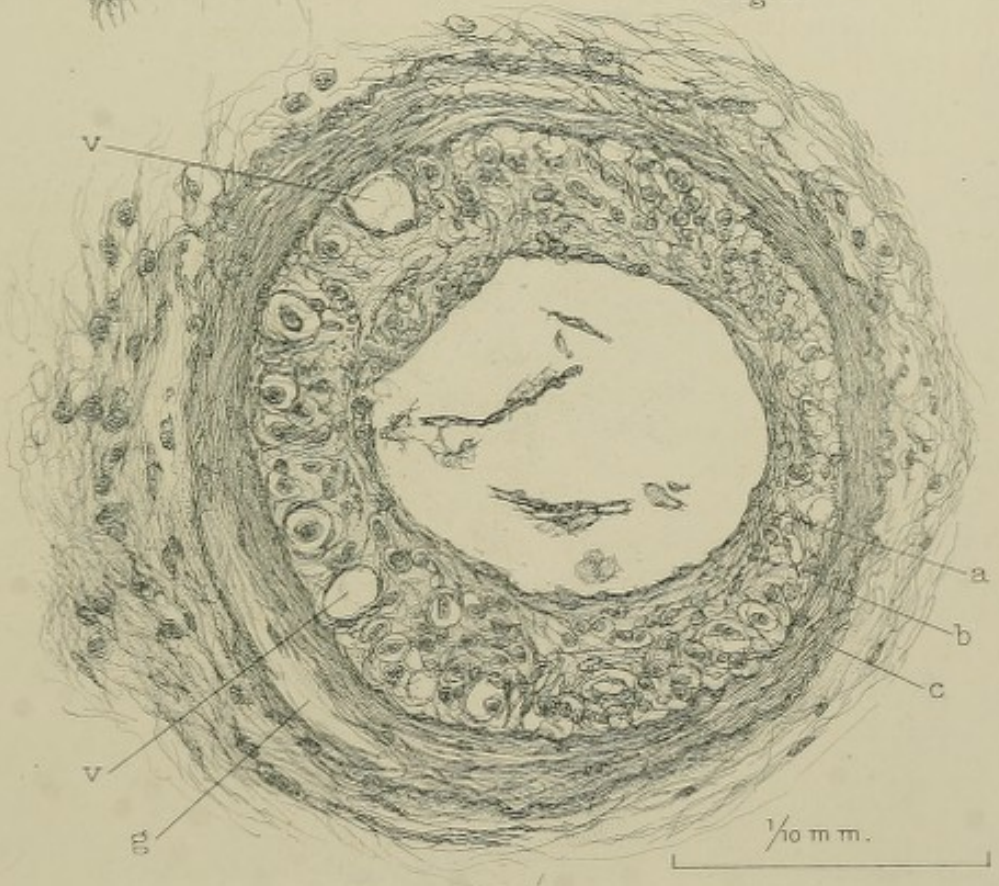


FIG. 24.—VASCULARITY OF THE NEW GROWTH IN ENDARTERITIS. (× 220.)

This drawing and Figs. 25, 26, and 27 are from a set of serial sections of the artery represented by Fig. 23. A vessel (*v*) at *d* is breaking through the muscular coat (*m*) of the artery to supply blood to the new growth (*i*).

FIG. 25.—VASCULARITY OF THE NEW GROWTH IN ENDARTERITIS. (× 220.)

The section next below that shown by Fig. 24. The supply-vessel (*v*) is here seen to have passed quite through the muscularis (*m*) of the artery. *f* is a large blood-cell lying in the calibre of the supply-vessel after its passage into the new tissue (*i*). It is important to remember that there is no connection between the supply-vessel (*v*) and the calibre of the artery.

FIG. 24.

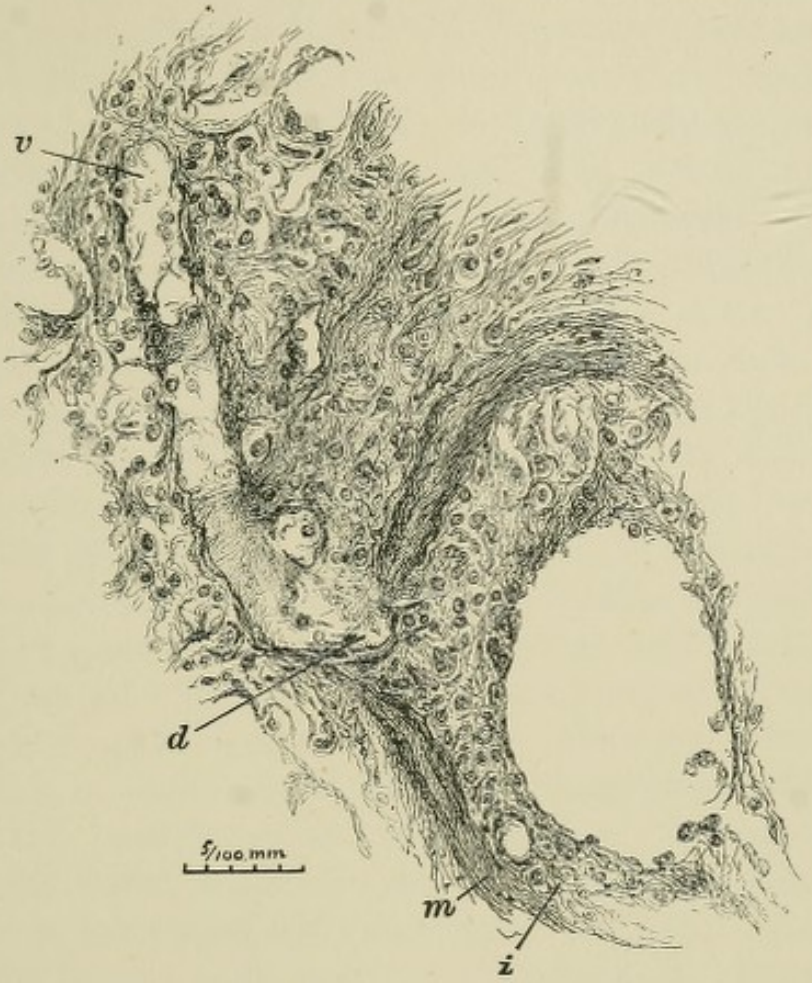
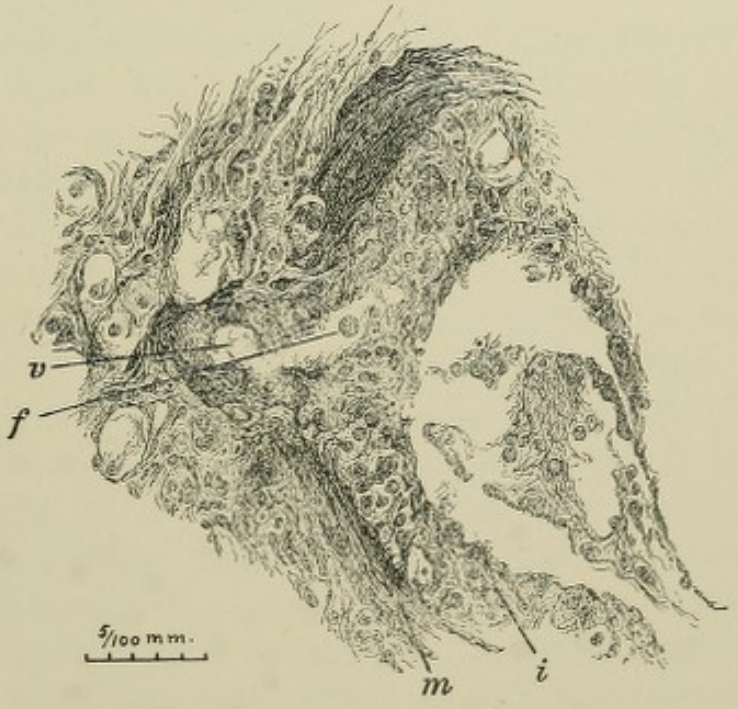


FIG. 25.



vessels in the new tissue having been observed, a series of sixty-eight sections was prepared, to ascertain if anything could be found tending to prove more positively that these vessels are capillaries, as they appear to be. The results will be most easily comprehended from the figures and a detailed description. Fig. 23 is an arteriole in which a large amount of new tissue had developed inside the plicated membrane, which is distinctly visible as a zigzag line around the greater part of the circuit. This new growth, which is of the intima, is of such extent that it forms a layer of greater thickness than the muscularis and the adventitia together. The diseased intima, the growth of which has reduced the calibre of the arteriole to a very small proportion of what it once was, is made up of tissue resembling that shown in Fig. 21, so far as the appearance of the cells is concerned. These have large nuclei and distinct external cell-walls, the protoplasm, represented as pure white, being structureless and unstained. The feature of special interest, however, is the presence of two blood-vessels (Fig. 23, *v*) in the overgrown intima. Their walls, formed of thin endothelium in which can be seen a few flattened nuclei (see description of Fig. 23), have the structure of capillaries. The plicated membrane, as already stated, is distinguishable around the greater part of the circuit as a somewhat indistinct, wavy line, and outside of it is the irregular and much degenerated muscular coat. Between the muscularis and the adventitia is an outer plicated membrane, which is sometimes present (see Fig. 13). The adventitia does not present any points of interest. Figs. 24 and 25 represent two adjoining sections from the series of sixty-eight. Only half of the arteriole is included in these, as they are intended to demonstrate the growth of nutrient vessels in the new tissue. Fig. 24 shows the entrance of a vessel into the thickened, diseased intima. This vessel is to be classed as a large capillary or a small arteriole, and its walls are similar in structure to those already described (see page 51, and Fig. 19) as common to newly developed vessels. The new vessel, to reach the diseased intima, passes directly through the muscular coat. It must be specially remembered that the passage of a blood-vessel through or even into the muscular layer of an artery never occurs in the natural condition. Fig. 25 is the section cut directly beneath Fig. 24, and it shows the nutrient vessel after it has passed farther into the intima. There is a large cell lying in the calibre which must be an embryonal blood-corpuscle, as it is not like anything belonging to the solid tissues. That this vessel (Figs. 24 and 25, *v*) was a nutrient supply-

vessel, and not merely a branch passing out from the main arteriole, is fully proved by Figs. 24 and 25 and the sections which were cut beneath them. In Fig. 25 the capillary is seen to be opening into the tissue forming the thickened intima, and in the sections below, of which it has not been thought necessary to have drawings made, it can be seen to divide into two branches which disappear in the tissue of the intima. These branches have thin walls of endothelium, and there is not the slightest indication anywhere of a connection with the calibre of the main arteriole in whose walls the whole system lies.

The development of blood-vessels in the tissues of the embryo has already been adverted to. Figs. 26 and 27, which are from the same series of sections as the preceding, contain spaces in the thickened and diseased intima, which are developing blood-channels like the blood-islands which are always to be found at a certain stage in embryos. In Fig. 26 is seen a space (*b*) which contains several cells. This is undoubtedly a blood-island with embryonic corpuscles; for its appearance precludes the possibility of its being a large multinucleated cell, and sections from above and below it show that it is an isolated space, and not a cross-cut of a capillary. There was no continuity of a channel either above or below; the space was therefore isolated,—a true blood-island. In Fig. 27 is a space containing a three-cornered body with minute threads attached to its ends toward the right. This answers exactly to the descriptions * of the protoplasmic processes from which capillaries are developed and with which the endothelial walls are continuous. That the spaces in Figs. 26 and 27 are developing blood-islands as described does not seem to admit of doubt, and it is likely also that the nutrient vessel (Figs. 24 and 25) was still unconnected with the general blood-stream, and therefore was not sufficiently developed to contain circulating blood, for the series of sections failed to demonstrate its connection with any other vessels.

Atheroma is a term used to designate many varieties of vascular disease. It has been employed most frequently to describe two common lesions of the inner surface of arteries, the elevated yellowish areas and the ulcers, these being named respectively atheromatous patches and atheromatous ulcers. Recent knowledge of the processes of vascular disease has outstripped accepted classifications and names, and this makes it difficult to discuss such disease except by describing minutely any particular lesion which is under discussion and thus

* Piersol's Histology, loc. cit.

FIG. 26.—DEVELOPING CAPILLARY IN NEW GROWTH OF THE INTIMA OF AN ARTERY. (× 220.)

Section from the same series as the two preceding figures. *b*, a blood-space containing cells. This might be taken to be a multinucleated cell. It answers the description given by embryologists of the blood-islands of Pander. In the sections above and below this there is no connection with any channel to show that *b* is a cross-section of an ordinary blood-vessel.

FIG. 27.—DEVELOPING CAPILLARY IN NEW GROWTH OF THE INTIMA OF AN ARTERY. (× 220.)

Section from the same series as the preceding. *b*, a blood-space in which is seen a small triangular body that answers exactly to the histological descriptions of the protoplasmic processes seen in the early stages of the development of capillaries. One point of the triangular process appears to be breaking through the muscularis (*m*), as if the capillary was growing in that direction, while to its two other points are attached fine threads which look like the endothelial walls of a capillary; *m*, the muscular coat; *i*, the overgrown intima; *p*, the plicated membrane visible in a part of the circuit of the artery and marking the separation of the muscular coat (*m*) from the diseased intima (*i*).

FIG. 26.

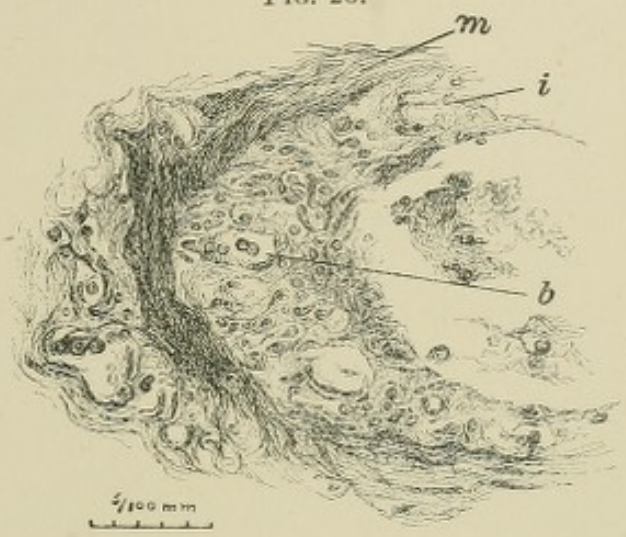


FIG. 27.

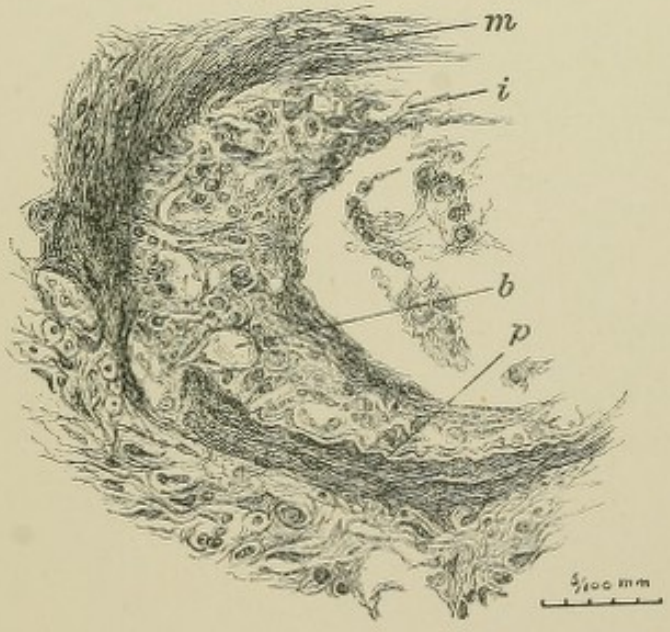


FIG. 28.—AN ATHEROMATOUS AND CALCAREOUS RADIAL ARTERY. (× 20.)

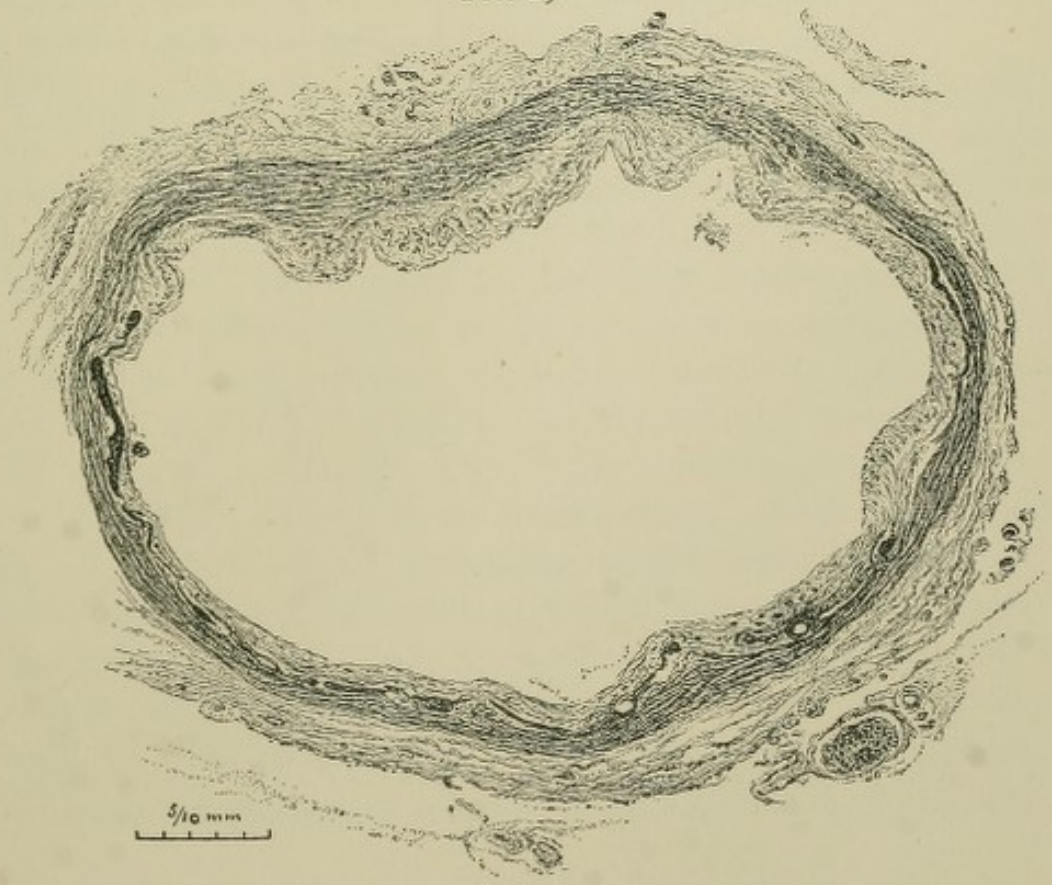
From a man fifty-seven years old who died of Bright's disease. The vessel is degenerated to such a degree that none of the ordinary boundaries are distinguishable. The wall is composed of grumous and coarse fibrous material, and it contains a number of cavities. Some of these spaces were filled by chalky deposit, which was removed with weak hydrochloric acid before the section could be cut, and others are atheromatous abscesses. The very dark-colored areas represent structureless material. The distinction of muscularis from intima having disappeared, it is impossible to know in which of the coats the disease originated.

FIG. 29.—AN EARLY STAGE OF ARTERIAL ATHEROMA. (× 26.)

An artery from the anterior surface of the medulla oblongata of a man fifty-seven years old who died of Bright's disease. The seeming great thickness of the wall at the top in the picture is probably due to twisting of the vessel so that the section is oblique instead of directly transverse. The three tunics are easily distinguished, and it is evident that the intima is a good deal thickened. The most striking peculiarity, to show which the illustration was made, is the degeneration which has taken place between the intima and the muscularis. At the junction of these two coats are several small cavities and irregular dark lines which represent structureless tissue. The situation of these minute atheromatous abscesses and structureless areas shows that in this instance the whole of the process of degeneration began at the junction of the intima with the muscularis. This is the situation occupied by the plicated membrane in healthy vessels.

FIG. 28.

FIG. 29.



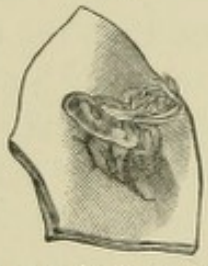
avoiding the application to it of the names in common use except in their most broad and general sense. One may speak of an aneurism, for instance, without risk of being misunderstood, and the application of the term atheroma to such patches and ulcers as have been mentioned receives universal acceptation. The difficulty of finding names by which satisfactorily to designate particular arterial lesions after they have been studied and their nature ascertained is plainly reflected in standard pathological text-books. Ziegler,* for instance, gives a clear and practical description of the pathological anatomy of arteries, but after reading it the impression is left upon the mind that the naming of the different lesions is very inadequate. Clinical and pathological evidence seems to tend to show that most of the ordinary lesions of vessels which vary so greatly in appearance are nevertheless closely related, and are often only the varying results of a common underlying process. During life arterial disease is discovered more frequently in the radial than in any other artery, owing to the common practice of feeling the pulse at the wrist. There is no evidence that the radial is more prone to disease than the other large arteries, but it is undoubtedly a good vessel to study post mortem, because it is so often known during life to be diseased. So far as concerns post-mortem appearances the condition of the aorta is best known, for in making autopsies the heart is almost always examined, and this cannot be done without the condition of the aorta being forced upon the attention of the pathologist.

Fig. 28 represents the radial artery of a man fifty-seven years old who died of Bright's disease. So much calcareous material had been deposited in the tissue that it was necessary to decalcify it with acid before a section could be cut. Within the calibre lies a large amount of clotted blood. The walls of the vessel are degenerated to such an extent that no differentiation of the layers is recognizable and the tissue appears structureless. There are numerous nearly empty spaces; these are either atheromatous abscesses or the spaces occupied by calcareous deposit. The picture presents a type of arterial degeneration in its most extreme development. From such an artery as Fig. 28 it is, of course, impossible to determine in which of the coats the disease had its origin, or which of them grew to form the thickened diseased wall. Fig. 29 is an artery from the anterior surface of the medulla oblongata of the man from whom Fig. 28 was obtained. It illustrates two points,—the occurrence of thickening of

* Lehrbuch der pathologischen Anatomie, zweiter Band, Seite 52. Jena, 1892.

the intima without involvement of the other coats, and that the degeneration which had begun originated at the junction of the intima and the muscularis. The greater thickness of the upper wall is here owing to obliquity of section, and not to actual thickness of the wall (see description of Fig. 29). The demonstration made by Fig. 29 of the seat of origin of the degeneration is important, and it is not very common to find an artery at just the stage to show it. The minute open spaces depicted are atheromatous abscesses, and the long, dark-colored lines represent material which has become structureless from degeneration. Both the abscesses and the structureless tissue lie directly between the intima and the muscularis, in the region occupied by the plicated membrane in healthy vessels. In this vessel the plicated membrane has been completely destroyed. Figs. 7, 28, and 29 are all from the same patient, and they demonstrate, first (Fig. 7), thickening of the intima in its earliest stage; second (Fig. 29), the beginning of degeneration, and, third (Fig. 28), arterial disintegration with calcification in its greatest development.

FIG. 30.



An excrescence upon the inner surface of the aorta, from a woman thirty years old who died of Bright's disease; drawn of natural size. The excrescence has much the shape of a vegetable fungus, being composed of an expanded top, to which are attached fine threads that floated in the blood-stream. The growth sprang from a pedicle which passed like a root through the wall of the aorta, the wall having been eaten away by ulceration to allow the passage of the pedicle. This growth appeared to be of similar nature with that represented in section and enlarged in Fig. 31. It differs, however, in that the opening through the aortic wall is smaller and the excrescence larger.

Figs. 30, 31, and 32 are views of two growths upon the inner surface of the aorta near the heart. The case was one of an irregular form of Bright's disease in a woman thirty years old. Fig. 30 is one of the growths, natural size. It is an excrescence having much the shape of a toad-stool, the stalk rising from a hole or depression in the aorta. Fig. 31 represents a section through the other growth, and it shows that there was less projection into the calibre of the aorta, but that the intima and the muscularis were ulcerated completely through, allowing the blood to burrow into the adventitia so as to form a small dissecting aneurism. The free ends of the muscularis have twisted so that they project into the calibre of the aorta. There are two or three of these projections, and each of them is formed of a basis of muscular tissue upon which has been deposited a covering of material which examination under higher amplification shows to

FIG. 31.—EARLY STAGE OF AORTIC ANEURISM. (× 10.)

From a woman of thirty years who died of Bright's disease. The intima (*i*) and muscular coat (*m*) have been broken through by the process of disease and a small dissecting aneurism formed whose wall is composed almost entirely of adventitia (*a*). There are several cauliflower excrescences (*g*) which projected into the calibre of the vessel. The base or centre of each of these is a shred of the muscular coat, while the outside portion is clot. *f* is an area represented in Fig. 32 more highly magnified. Fig. 30 represents another aneurism which was close to the one here depicted.

FIG. 32.—EARLY STAGE OF AORTIC ANEURISM. (× 105.)

Enlarged view of the region *f* in Fig. 31. From *a* to *b* is one of the shreds of the muscular coat (see description of Fig. 31) forming the centre of the excrescence. The drawing shows that at *a* is a well-organized tissue, while at *b* it is only clot, and that the transition from organized tissue to clot (from *a* to *b*) is so gradual that it is impossible to say where the one ends and the other begins. Everything included in the drawing except the band (*a* to *b*) is clot, and it is all ill defined except at *d*, where it has assumed curious forms.

FIG. 31.

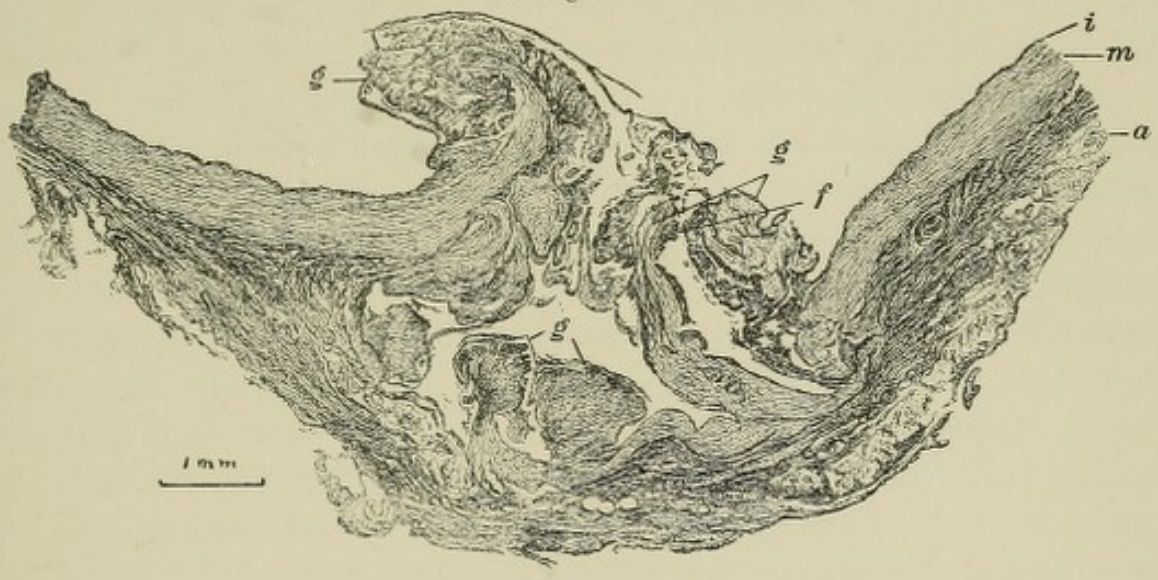


FIG. 32.

be partly clot and partly inflammatory growth. Fig. 32 represents a portion of one of the projections or fungous growths from Fig. 31 (see descriptions of Figs. 30 and 31). Centrally from bottom to top runs the core which springs from the muscular layer. This is composed at the lower portion (Fig. 32, *a*) of distinct fibres interspersed with nuclei, and is muscular tissue distorted and changed in appearance by the ulcerative process to which it was subjected. Toward the top the core becomes of less and less definite structure, until finally (Fig. 32, *b*) it is simply clot. The material upon both sides of it is formed of clot, composed of corpuscles more or less disintegrated and strings of fibrin, and at places this clot has assumed curious circular forms (Fig. 32, *d*). Strange effects are often produced in clots, caused by the shrinking that always occurs as a result of the efforts of nature to remove them.

These two growths show that a number of disease-conditions which are commonly considered to be distinct are in truth closely related, if, indeed, they are not merely variations of the same process. The ulceration must be classified as atheromatous, and the sac in the fibrous coat as an aneurism, for the intima and muscularis were broken through and the vessel-wall already a little pouched upon its outer side. The tendency to growth like a toadstool is peculiar; the same disposition to proliferation is equally plain in the second growth, although it was less extensive. That the process of inflammation was an important factor in the production of the disease is certain, for nothing else could have caused the ulceration and the extensive blood-clotting upon the cut ends of the muscular coat. An interesting feature is that the connection between the clot and portions of the arterial tissue is so intimate that it is impossible to say where the one ends and the other begins. The fact that clots within vessels are not mere deposits upon the inner surface which may be removed, leaving the tube in exactly its former state, is well known. Threads of tissue grow out from the inner wall of the artery, and may be seen running through the clot, binding it firmly in the situation in which it was formed.* It would be unreasonable to believe that a vessel suffers no injury from the formation of clots within it, when it is known that outgrowths of tissue from the intima into the clot are a common accompaniment of the process. It is my belief that the formation of clots within the

* Pathologische Anatomie von E. Ziegler, Jena, 1892, zweiter Band, Seite 59: "die thrombotischen Auflagerungen bereits von der darunterliegenden Intima mit Bindegewebszügen durchwachsen sind."

arterial system is of very frequent occurrence, and that it results from a great many of the diseases and even disorders to which men are subject. It would be interesting to know what influence clot-formation may have in the production of the thickenings of the intima of arteries, especially in old persons and those past middle age. In connection with the growths that have been under discussion the appearances presented by Fig. 29 (see description) suggest the question, What would have been the result of a greater duration of life of the patient? The minute atheromatous abscesses and areas of degeneration at the junction of the intima and the muscularis could not have remained as they were, but must have increased in size until they ruptured and the cavities discharged their contents inwardly into the blood-stream or outwardly through the fibrous coat, or it would not seem surprising that the end of such a process should be the perforation of the arterial wall and the discharge of blood into the cranial cavity to produce apoplexy.

The condition which has been described as tubercular arteritis is represented by Fig. 33. The vessel looks as if it was being overwhelmed by the infiltration of cells which are entering from its outside. There is nothing that suggests the existence of disease of truly vascular origin, but the appearance is that the vessel, as it happened to lie in a tubercular area, was involved by the disease in the course of its progress. Tubercular arteritis, therefore, has no real existence, and the condition is nothing but the involvement of the vessels by the cellular infiltration, which is the characteristic of the tubercular process everywhere.

Veins.—Much less study has been bestowed upon veins than upon arteries, and this is especially the case in regard to their morbid anatomy. It is more difficult, therefore, to form opinions about the veins than about arteries, for there is in comparison so little pre-existing information to serve as a basis upon which to build. The literature of disease of arteries, both that found in text-books and that found in periodicals, is immense, while that of disease of veins is comparatively meagre. Nevertheless, certain facts about the veins are thoroughly well established, and the most important of these is that veins are, from their very nature, less subject to disease than are arteries. Of the four parts of the circulatory system, the heart, the arteries, the capillaries, and the veins, the veins alone perform a passive function. Their sole work is to receive the blood from the capillaries and return it to the heart. This is accomplished by forces which even at the present

FIG. 33.—TUBERCULAR ARTERITIS. (× 220.)

From a man forty-six years old who died of phthisis: a minute arteriole lying in a tuberculous area of the lung. There is some clot lying in the lumen of the vessel, the walls of which have lost all differentiation of coats. The striking feature is that the inner portion of the vessel is that which is most nearly natural, while from the outside it has been invaded by the infiltration of the round cells which constitute the greater portion of the tuberculous tissue. The whole appearance is that the process began outside and was proceeding thence toward the inner portion, and was therefore not truly vascular in its origin.

FIG. 33.

time are by no means thoroughly understood. Further than this, the fluid they carry is a waste product which they receive after it has accomplished its function, and is lifeless, fit only to be returned to the great mill from which it came, to be worked over into renewed activity. There is no more common disorder as life advances than varicose veins of the legs, and it has been my experience to find that in cases where the arteries are greatly diseased the veins partake in the process. It seems as if their passive nature pursues them even in their states of disease, and that they become diseased most often when some other and more actively disposed part of the organism starts the train. When, for instance, a large artery like the femoral becomes thick and rigid from the deposit of calcareous material, its accompanying vein will usually be found to be similarly diseased. This fact I discussed in a paper published some years ago,* and showed that atheroma and calcareous deposit may occur in a vein and change it so greatly that it cannot be distinguished by its appearance alone from an artery. Figs. 34 and 35 are reproduced from that paper. All the coats are thickened, the intima of the vein being thicker than that of the artery (see descriptions, Figs. 34 and 35). Fig. 36 represents a section of the vena cava of a man fifty-seven years old who died of Bright's disease, with extensive fibrosis and disease of the arteries. The vena cava is seen to be greatly thickened, degenerated, and of a loose texture, and some of its vasa vasorum are almost closed from endarterial thickening (see description). Figs. 37 and 38 show a curious and interesting instance of disease of a vein. The first represents a portion of a vein in transverse section, and was published in the paper just mentioned. Lying opposite each other in the wall are two growths. One of these is represented under high amplification by Fig. 38. There are irregularly circular nests of cells, which are in many respects more like epithelium than like connective tissue. The tendency of cells to arrange themselves in this manner in nests in young and in rapidly growing tissues is very common, and is frequently to be seen in skin cancer, in the healthy skin of infants, and in embryological tissues, and I have often seen such nests in the walls of diseased arteries and occasionally in diseased heart-valves. The resemblance to the cell-nests considered so characteristic of epithelioma of the skin is very close, showing that great care must be

* A Study of the Arteries and Veins in Bright's Disease, by Arthur V. Meigs, Transactions of the College of Physicians of Philadelphia, June 6, 1888; published also in The Medical Record, New York, July 7, 1888.

exercised in pronouncing an opinion from microscopical appearances alone in regard to the malignancy of any particular growth. The disease of veins offers an interesting field for study, especially from the side of pathology, and it is one which has as yet been very imperfectly investigated. The facts that have been adduced tend to show that the veins are usually involved when the arteries are extensively diseased, but it is probable also that it will be found, even after exhaustive study, that disease of the veins, unless more extensive than is common, plays a less important part than arterial disease. The passive nature of the function of the veins, and the fact that the flow of the blood is from a great number of small tubes into a constantly decreasing number of greater size, make the friction within the system an always decreasing one, and render them less liable than arteries to disease.

Capillaries.—The normal and pathological anatomy of capillaries will be discussed in connection with disease of the heart (page 63), in which organ I have studied them with more profit than in any other part of the body. Of the three kinds of vessels of which the vascular system is composed, the capillaries are the most difficult to follow and understand. This difficulty is because they cannot be examined to any advantage without high amplification, and, besides this, the material of which they are composed is of such delicate structure that they are often clouded by the decomposition of the tissues which takes place before or after death. In persons dead of typhoid fever and other diseases which cause great disorganization of the blood and general softening of the tissues, microscopical examination often yields very unsatisfactory results in all respects, and delicate parts like capillaries cannot even be seen.

It is difficult to conceive anything that could be more important to the science of medicine than a complete comprehension of the anatomy of the blood-vessels and an understanding of their diseases. Such information would seem to promise more for the advancement of our knowledge of the origin of disease, and especially of chronic disease, than anything else. Everything, therefore, that adds to the sum of knowledge of this subject must be of great value. The illustrations and description of the anatomy and diseases of blood-vessels which have been given furnish a good general idea of the forms of changes which are most common in chronic disease. This must be the case because they are representative of a large collection of sections gathered in the course of many years in hospitals and private prac-

FIG. 34.—VEIN AND ARTERY SHOWING THICKENING OF THE INTIMA AND GENERAL ATHEROMA. (× 6.)

Femoral artery and vein from an elderly man who died of Bright's disease. Both vessels were converted into rigid bony tubes by calcareous deposit, and had to be treated with acid before sections could be cut. The artery looks broken, the intima is irregularly thickened, and there are spots of degeneration of the muscular coat. The intima of the vein is greatly and irregularly thickened. At one place the intima and muscularis are broken loose from the fibrous coat. This and the breaks in the artery either resulted during life from the deposit of the calcareous material or occurred after death in removing the vessels, which were so rigid and firmly fixed that it was difficult to cut them loose. Fig. 35 shows part of the vein more highly magnified.

FIG. 35.—DISEASED VEIN. (× 22.)

A portion of the vein shown in Fig. 34, more highly magnified. *i*, intima; *m*, muscularis, and *a*, adventitia. Such extensive disease with great thickening of the intima is probably not common in veins.

FIG. 34.

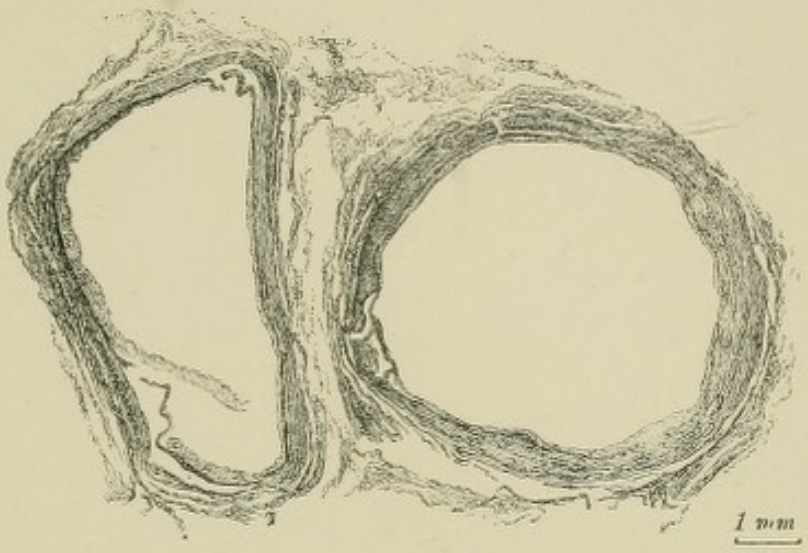


FIG. 35.

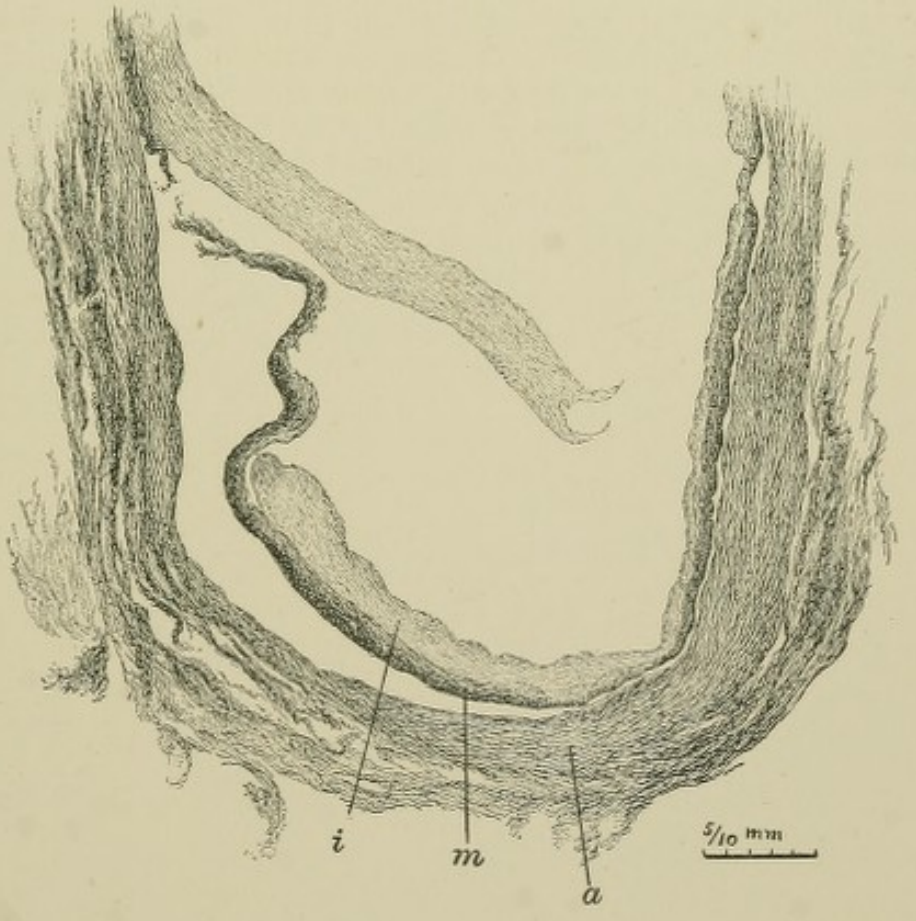


FIG. 36.—THICKENED AND DEGENERATED VENA CAVA. (× 44.)

From a man of fifty-seven years who died of Bright's disease. *e* is a section of the wall of the vena cava magnified about four diameters; *f* is its inner and *g* its outer surface. At *g* the outer portion of the adventitia has been somewhat separated in the process of preparation. The dotted lines indicate the portion of vena cava included in the larger drawing below (× 44); *i* is the intima, which is shredded out and broken as the result of disease. Below, the muscular coat is very loose-meshed, and at *n* is replaced by a tissue of different texture. The muscular layer is much thicker than natural. The fibrous coat is very thick and loose-meshed, and there are vessels in it (*v*). The two vessels (*v*) in the separated portion of adventitia are so greatly thickened inwardly as to be almost closed.

FIG. 36.

FIG. 37.—GROWTHS IN THE WALL OF A VEIN. (× 50.)

Part of a vein in the fat layer of the heart of a man of fifty-four years who died of heart disease. The vessel was somewhat flattened in course of preparation, and therefore does not appear as circular. There are two growths, one upon each side of the vein; one of these (*d*) consists of three somewhat circular bodies, and it is represented more highly magnified by Fig. 38.

FIG. 38.—GROWTHS IN THE WALL OF A VEIN. (× 250.)

Enlarged view of the growth (*d*) shown in Fig. 37. There are three circles or whorls, and the cells are very like epithelium.

FIG. 37.

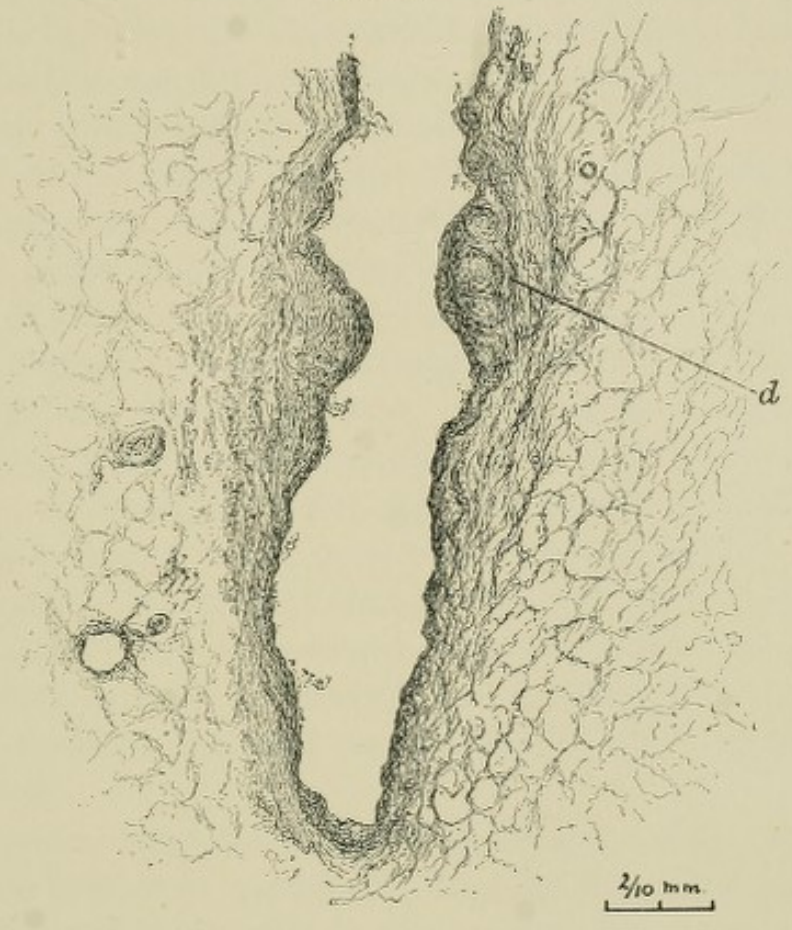
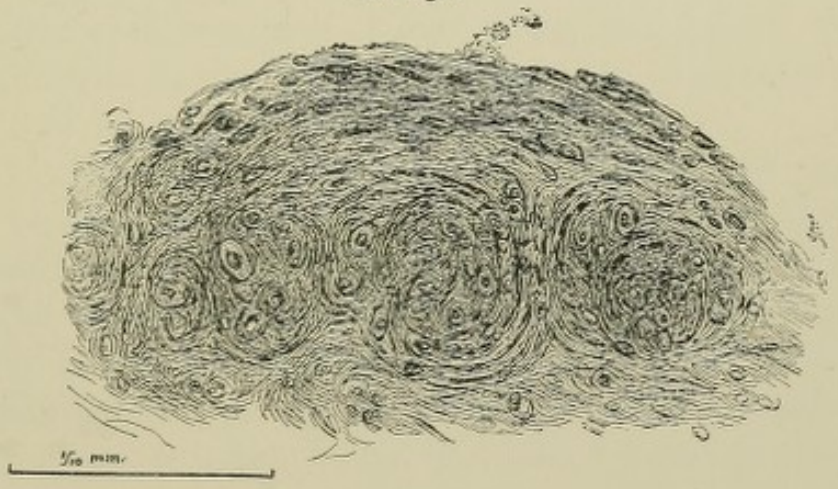


FIG. 38.



tice. Clinical observations of the same cases were made concurrently, and a great variety of diseases, especially of chronic diseases, is represented. In addition to the graphic demonstration of lesions of blood-vessels, which includes the observation that the intima is immeasurably more often the seat of disease than are the two other coats, several very important conclusions are reached.

The blood-vessels always undergo changes with the advance of life, and these changes are exactly imitated by others occurring in younger persons as a result of disease; they consist principally of thickening of the coats of the vessels, especially of the intima. If the thickening be extensive it always reduces the size of the calibre, and this inevitably interferes with the vessel's function. As age and disease produce identical effects, it follows as a corollary that it is frequently difficult or impossible to know, from the appearances alone, whether lesions are those which belong to age or are the result of disease. In studying blood-vessels, both microscopically and with the unaided eye, the pathologist always has to contend with this difficulty of deciding whether departures from the histological standard are due to disease or are what must be expected to be present in consequence of the passage of time.

Blood-vessels are especially prone to disease, owing to their function,—the distribution of the blood. Besides this, they are present in all parts, and therefore are sure to come within the range of every disease that attacks the body, no matter what may be its locality. As blood-vessels exist everywhere, they are likely, owing to their continuity of structure, to transport disease along their walls. This takes place in addition to the carrying of disease from place to place by the blood itself, which probably is effected very frequently.

A most important fact is that there are no peculiar histological changes of blood-vessels belonging specifically to any one disease. Nothing could more forcibly illustrate this than the truth which is coming to be pretty well known, that syphilitic endarteritis is in every respect identical with endarteritis arising from various other causes. The endarteritis deformans which is so common in old people, and which is often found in various parts of the body in Bright's disease and in chronic heart disease, is frequently identical in all its physical characteristics with that which is caused by syphilis. It is not long since it was believed that certain arrangements of the cells and certain forms of thickening of the walls of arterioles could be produced only by syphilis, and that it was not difficult for any one who

had attained the requisite degree of skill to recognize them by their peculiar appearances alone. It is now, however, beyond question that there are no specific histological lesions which belong to any particular disease. Pathological lesions, both gross and microscopical, can help to a conclusion of what disease is being dealt with only if they are considered in a general way; the state of the blood-vessels and changes in different organs must be judged collectively if any stable conclusion is to be reached.

The tendency to the development of a blood-supply in new tissues is well known. The growth of such blood-vessels has been extensively studied, and their peculiarities of origin, even in clots, thoroughly elaborated. The formation of clots and their organization are probably the beginning of most new tissues developed as a result of disease, if they are rapidly produced. When new tissue is developed slowly, the fibroid cicatricial tissue of which it is composed probably arises without any clot-formation as the first step. However this may be, it is a fact that even in adults the capacity for development has not been extinguished, and under the stimulus of disease is often set in motion. Of this no more striking proof could be adduced than is furnished by the new tissues which are shown by the illustrations. The tissue which developed between the two layers of adherent pericardium (Figs. 18, 19, and 20) and in the lung-arteriole (Figs. 23 to 27), thickening it inward, and the vessels developed in them both, show the general characteristics of the process in a most satisfactory manner. An extraordinary and, at present, entirely inexplicable feature of the development of new blood-vessels is the occasional formation of solid rods (Figs. 15 and 20) instead of tubes. It appears as if the growth that is started by disease is so excessive and uncontrolled that it defeats the purpose for which it arose, and produces a useless solid rod where a tube to carry liquid is needed. This strange phenomenon is worthy of careful consideration, although as yet no meaning can be attached to it. The striking similarity of the processes of development of blood-vessels in new tissues under the stimulus of disease and the healthy growth of blood-vessels in embryos has been pointed out (Figs. 23 to 27).

The fact that malignant growths may be closely imitated by arrangements of the cells occurring in disease undoubtedly non-malignant (Fig. 38) has an important practical bearing. It shows that it may be difficult to conclude, under circumstances which not infrequently arise, whether in a given case disease is malignant or benign.

CHAPTER V.

THE HEART.

In the pursuit of pathological studies directed especially to the investigation of Bright's disease, vascular changes, and heart disease, and the relations of these morbid processes to one another, I have examined a great many hearts. The number of human hearts of which sections are in my collection is eighty-nine, and in most instances these are accompanied by full clinical histories of the patients. The causes of death include violence and many different diseases, and the ages ranged from an early embryological period to three weeks after birth, and upward to old age.

Before proceeding to discuss disease of the heart, it is necessary to describe a portion of its anatomy. The blood-vessels differ somewhat from those of any of the other organs. Upon this subject I have already published essays.*

Upon the surface of the heart there are numerous arteries and veins of ordinary structure; they have three coats and the muscularis has circular fibres. Though veins with three coats are always present on the surface, they are rare in the walls of the heart, where three coats are found only in veins of large size, the smaller return vessels being composed of a single layer of endothelium. On the other hand, the arteries have three coats, the circular muscular fibres being easily distinguishable even in arterioles but little larger than the capillaries of least diameter.

The capillaries of the human heart differ in two ways from those of other parts of the body: they penetrate the muscular fibres, and some of them are larger than those found elsewhere and they are differently arranged.

The illustrations (Figs. 39 and 40) are drawings which were made with the camera lucida; they are from sections of two human hearts.

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* The Microscopical Anatomy of the Human Heart, by Arthur V. Meigs, Transactions of the College of Physicians of Philadelphia, April 1, 1891, and the American Journal of the Medical Sciences, June, 1891. The Penetration of the Muscular Fibres of the Human Heart by Capillaries, and the Existence in that Organ of very large Capillaries, by Arthur V. Meigs, Journal of Anatomy and Physiology, vol. xxxiii.

One is that from which the illustrations of my original paper were made, and it shows the heart of a negro woman forty years old, who died from the effects of burns. Some pieces of the organ were preserved in Fleming's solution, and others in seventy per cent. alcohol, and they were stained in bulk with borax-carmine and embedded in paraffin. The other heart is that of a man thirty years old, who died of lead encephalopathy. When the autopsy was made, the heart was injected with a solution of Berlin blue. Pieces of suitable size were placed in preservative fluid, some in seventy per cent. alcohol and others in formaldehyde solution. The tissue was afterwards stained in bulk with borax-carmine and embedded in paraffin.

Very large capillaries are found in the human heart, and such vessels are shown by Fig. 39, *A* and *B*. It is not common, however, to find minute veins of the ordinary structure in company with the arterioles in the deepest portions of the muscular substance of the heart. Here, when an arteriole is accompanied by an efferent vessel, this vessel is single coated and composed of endothelium, being exactly like the smallest capillaries, except in size. These peculiar large capillaries are found not only in company with arterioles, where they exercise the function usually performed by veins, but also alone. Where they are alone, it is impossible to be certain whether their function is afferent or efferent. It may be that arterioles are less numerous in the heart than in other tissues, and that their place is taken by the large capillaries. These capillaries are so numerous and of such large size that it seems likely they perform the function of reservoirs.

The distribution of the capillaries in the muscular substance of the heart is well known up to a certain point; histologists thoroughly understand that the arterioles have their termination in capillaries which, after ramifying among the muscular fibres, terminate in veins. To say, however, that the whole circuit of the vessels has been thoroughly traced out as has that of the capillaries of the liver and kidneys would not be true, for in the works upon the subject the question is not pursued beyond the statement that the muscular fibres are richly supplied with capillaries. The capillaries run, of course, in all directions among the muscular fibres, parallel with and between them, at acute angles across them, and again often at right angles.

Transverse sections of muscle show the position and number of the capillaries and their relation to the fibres more graphically than any other preparations. In them many vessels present themselves

FIG. 39.—NORMAL CAPILLARIES OF THE HEART.

A (× 115). A section of heart from a negro woman forty years old who died from the effects of burns. A large capillary receiving many branches and surrounded by muscular tissue. The capillary and its branches are almost filled with blood-corpuscles. The capillary walls are distinctly visible, and contain many flattened endothelial nuclei.

B (× 42). A section of injected heart from a man of thirty years who died of lead encephalopathy. Not printed in two colors, because the essentials show equally well in black. *m*, muscular tissue; *a*, an arteriole; the solid black within its calibre is injection material. *v*, the accompanying vein to the arteriole *a*; the vein contains a little of the injection material: these two vessels are in a connective-tissue interspace; *c*, a large capillary: it contains a good deal of the blue injection material, which is represented by the heavily-shaded portions. These three vessels—arteriole, vein, and capillary—give a good idea of the character of such vessels in the heart. The great size of the capillary is the most striking feature.

C (× 420). From the same tissue as *A*. A section of heart cut transversely to the muscular fibres. The muscular fibres are of irregular shape. *d*, a capillary within a muscular fibre, its nucleus upon one side producing a resemblance to a seal-ring; *e*, a capillary within a muscular fibre; *f*, a capillary in an intermuscular space: its nucleus being included, it resembles a seal-ring; *g*, a capillary in an intermuscular space: its endothelial wall appears as a simple circle.

FIG. 39.

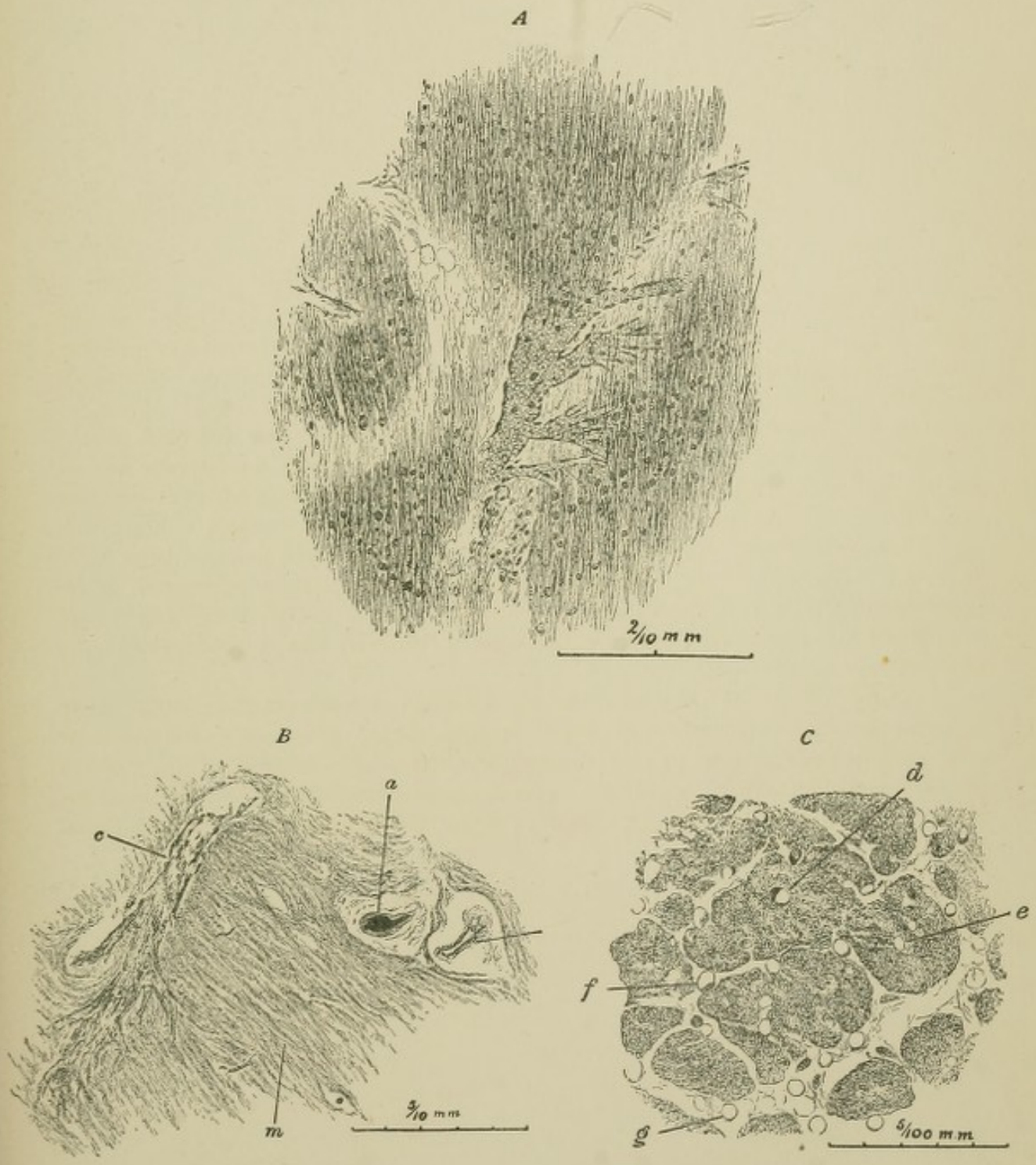


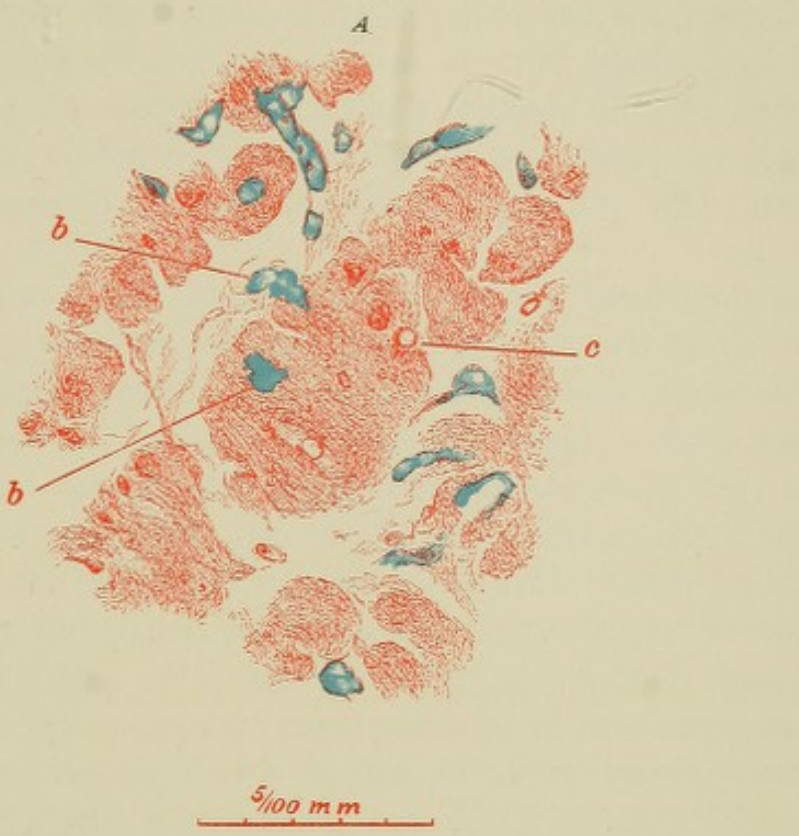
FIG. 40.—CAPILLARIES WITHIN THE MUSCULAR FIBRES OF THE HEART. (× 420.)

A. From a man thirty years old who died of lead encephalopathy. The cardiac blood-vessels were injected with a solution of Berlin blue; the tissue is red. A section of papillary muscle of the heart cut across the fibres: *b b* are injected capillaries, the one partially and the other entirely within the muscular fibres; *c*, a capillary which remains uninjected; its nucleus is included.

B. From the same tissue as *A*. *v*, a vein stained by the injection material; *b b*, capillaries whose precise situation cannot be defined. They cannot be said to be in intermuscular spaces nor to be entirely within fibres. The effect is as if the fibres were coalescing.

C. From the same tissue as *A*. *f*, a capillary in a fibre; *g*, a capillary in the centre of a very small fibre. This is perhaps the most convincing instance of the penetration of a muscular fibre by a capillary.

FIG. 40.



in the form of circles, or, if the section has been oblique, as elliptical. On the other hand, longitudinal sections may present an almost infinite variety of appearances. It would be impossible to give an adequate description of these varying appearances, but the mere mention of their existence is sufficient to remind any one who has given personal attention to the subject of the truth of the statement, and of the further truth that under the most favorable circumstances longitudinal sections of vessels are less satisfactory to study than are cross-sections.

The penetration of the muscular fibres by the capillaries is made perfectly clear by the illustrations; it is shown as well by the injected as by the uninjected heart. The two methods of demonstration supplement one another, because, in injected tissue, which has been stained, the blood-vessels and their situation are made very obvious by the contrast of color, but the details of the structure of the walls are obscured by the injection material, while, on the other hand, in the uninjected tissue, the structure of the blood-vessels can be seen with the utmost distinctness. Fig. 39, *C*, and Fig. 40 are scale-drawings of fields under the microscope of cross-sections of heart-muscle. It is easy to recognize the capillaries in the connective tissue, where they appear as minute circles with walls of exceeding delicacy. In a few of them the walls are much thicker on one side than on the other, resembling a seal-ring when looked at from the side. These thick spots show where the knife has cut through a nucleus in the endothelium of which the wall of the capillary is formed. A closer examination of the drawings, however, brings to light the fact that these empty circles are not to be seen in the connective tissue alone, for they exist also half embedded in the sides of the muscular fibres, and even in the very centres of the fibres.

This penetration of the muscular fibres of the human heart in the adult by the capillaries is a most striking and curious phenomenon, and it does not exist at an early embryological stage. The condition is therefore one of later development, but it is not yet known at how early an age it occurs. It would be interesting and useful to examine young human hearts to ascertain when capillaries are first found within the muscular fibres.

This aspect of the subject was considered by the late Dr. John A. Ryder. In discussing my original communication he said: "Many of the structures that we see in the adult organ are really developed during what embryologists speak of as the post-embryonic period.

When we reflect upon the way in which muscle universally develops, no matter whether it be in the salamander, the fish, reptile, bird, or mammal, we can see how, in the later stages of the development of the heart, such a thing as enveloping or inclusion of capillaries might occur. It is well known to every one who has made a cross-section of a developing muscle, that the fibrillæ appear as delicate threads embedded in the protoplasm forming the body of the muscle-cell. That is the type found in the highest form of muscular development. There are forms of muscular development in which the fibrillæ are developed in a continuous roll, and, as a result, the muscular fibre resembles a flat plate made up of parallel filaments. However, as we pass up in the animal scale, and particularly in mammals and birds, the muscular fibres become irregular in shape, and excessively numerous and closely packed together, with very little protoplasm between. When we remember that the multiplication of the fibrillæ seems to result from splitting up or multiplication of the fibres already present, we can understand that, as the muscular fibres grow in thickness, any capillaries that might lie beside them might readily be engulfed and covered in by the mutiplying fibres."

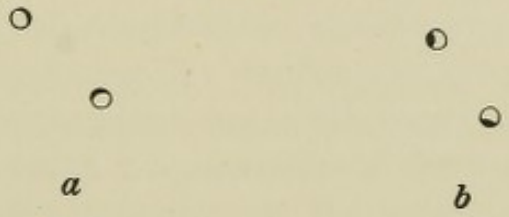
In a paper on the Histology and Histogenesis of the Heart-muscle Cell, by John Bruce McCallum (*Anatomischer Anzeiger Centralblatt für die gesammte wissenschaftliche Anatomie*, xiii. Band, No. 23, 1897), it is shown that during early embryological stages the muscle-cells are composed of undifferentiated sarcoplasm, even after the heart has begun to beat, in the case of the chick. The characteristic cross-striæ appear at a later period, and show themselves first in the more superficial layers of the heart. Therefore, it is evident that during the early stages the capillaries are not within the muscle-cells. McCallum quotes Schiefferdecker as saying that " after the tenth year yellowish-brown pigment is present at the poles of the nucleus in human heart-muscle. As age advances the pigment increases in quantity, and the granules become larger in size and of a deeper color."

It has been shown that the capillaries penetrate the muscle-fibres of the adult human heart, and it is certain that they are not within the fibres during the early stages of development; it is probable, therefore, that the capillaries get within the fibres by a process of inclusion, as was suggested by Ryder. The pigment which is found at the poles of the nuclei in the adult heart is absent during early life, and there is good reason to believe that it is somehow connected with the penetration of the muscular fibres by the capillaries. In future it must be

FIG. 41.—DIAGRAM SHOWING DISEASE OF CAPILLARIES OF THE HEART.

a, healthy capillaries which appear as circles with walls thicker upon one side; the thick portion occupying about one-third of the circuit. The thicker portion represents an endothelial nucleus cut across, the rest of the circle is delicate endothelium. In general appearance the capillary resembles a side view of a seal-ring. *b*, diseased capillaries. The nuclei have swollen so that they project into the vessel, reducing the calibre in size and making its shape irregular.

FIG. 41.



remembered that the nuclei in the muscular fibres are not all muscle nuclei, but that the capillaries, in penetrating the fibres, necessarily carry their own nuclei with them (Fig. 39, *C*, *d*, and Fig. 40, *A*, *c*). The presence of the large capillaries and the penetration of the muscular fibres by the capillaries indicate a provision for the blood supply of the heart even more bountiful than that of the other organs.

It is even more difficult to demonstrate disease of the capillaries of the heart than to trace out their distribution. Fig. 41 is a diagram which represents in contrast the natural appearance of heart-capillaries and a condition of them which is sometimes seen when the heart is diseased. In the diseased vessels the nuclei are swollen and changed in shape; they are enlarged and rounded so that they project into the lumen and obstruct it (Fig. 41, *b*). This condition is very common in Bright's disease, in heart disease, and in other forms of chronic disease. Fig. 42 shows two capillaries (*b* and *c*) which are narrowed. The effect in *b* is of an isolated piece of capillary drawn almost to a point at both ends, while *c* is a narrow neck in a capillary through which no natural-sized red blood-corpuscle could have passed. At the point of narrowing the capillary walls are slightly thickened. There are blood-corpuscles lying in this vessel close to the neck, which renders it easy to make a comparison of the dimensions. This drawing is a faithful representation of the appearances presented by the section from which it was made. It may be said that this narrowing of the capillaries is only the result of varying directions of the plane of section, but such does not seem to me to be the case. I believe it to be an actual condition of disease. None of the muscular fibre in Fig. 42 is healthy; most of it is granular in appearance and the cross-striæ are indistinguishable, but here and there are scattered fibrils in which the striæ are distinct. A curious and important result of disease is exemplified by the two bands of muscle (*x* and *y*, Fig. 42) which run at right angles to the rest of the muscular tissue included. A somewhat similar condition of disease is represented by Fig. 43, in which the muscular fibres are generally separated from one another by distinct intervals and form wavy lines, instead of being nearly straight and disposed in close bundles, as healthy muscular fibres of the heart are. The connective tissue between the fibres is evidently greatly increased, for in healthy heart-muscle there is but little connective tissue. The condition of disease is one of fibrosis; and the fibrous tissue has forced the muscular tissue apart, so that individual fibres stand by themselves and have been dragged about

and distorted. It is certain that muscle so distorted must have been very inefficient in its action. When it contracted there must have been great waste of energy in pulling the curved fibres, and great increase of friction from the side pressure upon the fibrous tissue. The explanation is that the growth of fibrous tissue was the cause; it insinuated itself into the muscle, pushing the fibres apart and dragging them out of line until they became isolated and wavy. Portions of muscular fibre so distorted as the two right-angled bands represented in Fig. 42 must have been useless, and the wavy fibres in Fig. 43 very inefficient.

A diseased state of the surface layer of fat of the heart is illustrated by Figs. 44 and 45.* The two pictures were drawn with the same amplification and under precisely similar conditions, and they show two different stages of disease, exhibiting a striking contrast. Condensation and fibrosis of the fat layer of the heart are very common in persons dead of various chronic diseases, and they are as often present in cases in which there had been no clinical evidence of heart disease during life as in those in whom heart lesions had been recognized. The changes are curious: the pericardium is thickened, and the fat so changed that, from having been composed of a collection of fine circles looking as if empty, the circles become more coarse and lose their discreteness, until finally there is only a confusion of fibrous threads, some straight and some curved, intermingled with circles, and sometimes there is even new-formed fibrous tissue rich in nuclei, as shown in Fig. 45. Fig. 44 illustrates an early and Fig. 45 a more advanced stage of fibroid condensation of the fat layer of the heart. Through this condensed and fibrous fatty tissue run the blood-vessels, and these also are diseased and more numerous than in healthy heart-fat. Whether the increase in numbers is due to the condensation, so that more vessels appear in a given surface in the section, or there is an actual increase of them, is impossible to say, but the evidence is in favor of an actual multiplication of vessels. In addition to their increase in number, the vessels are diseased; both the arterioles and the capillaries are thickened, and the capillaries in places (*x*, Fig. 44) are so bound up with the fibrous tissue that it is impossible to distinguish where the one ends and the other begins. The effect is as if a capillary ended abruptly in a mass of fibrous tissue; and it is not necessary to say that in nature no blood-vessel ever has an ending, but always leads on into another. In contrast with these two pictures Fig. 1

* Figs. 45 and 43 are from the same heart.

FIG. 42.—DISTORTION AND DISEASE OF THE MUSCULAR FIBRES OF THE HEART WITH NARROWING OF THE CAPILLARIES. (× 280.)

From a man of fifty-four years who died of organic heart disease. The drawing is of bands of muscular fibres, branching and ramifying capillaries of various sizes, and connective tissue. *m*, muscle, the greatest portion of which is granular in appearance, but here and there are fibrils which still distinctly show cross-striæ. *x* and *y*, muscular bands connecting at right angles two separated portions of muscle. Such an appearance is not natural in the heart, and can only be the result of forcible dragging apart of the fibres by the growth of fibrous tissue. *a* is a normal capillary filled with blood-corpuscles. *b* is a portion of a capillary which is too narrow to have performed its function, for its diameter is less than that of a red blood-corpuscle. *c* denotes a narrow neck in a capillary through which a corpuscle could not have passed; near the neck and lying within the capillary are blood-corpuscles. It may be thought that these narrowings were the result of the direction of section.

FIG. 43.—FIBROID HEART WITH DISTORTION OF THE MUSCULAR FIBRES. (× 60.)

From a man of forty-two years who died of organic disease of the heart. *a*, new and growing fibrous tissue forcing itself between the muscular fibres (*m*). The fibrous tissue is rich in nuclei. *c*, a capillary running at right angles to and passing sometimes above, and sometimes below, the muscular fibres. The muscular fibre is pulled open and distorted by the fibrous tissue to such a degree that its action must have been very inefficient. Fig. 45 is from the same section.

FIG. 44.—INFLAMMATION CAUSING CONDENSATION OF THE FAT LAYER OF THE HEART. (× 60.)

From a woman of forty years who died of organic disease of the heart: taken from a different portion of the same section as Fig. 1, which shows normal fat. *p*, thickened pericardium; *c*, a capillary forming part of a plexus which at *x*, adjacent to the pericardium, is diseased. The growth of fibrous tissue upon the under side of the pericardium is continuous with the capillaries, so that it is impossible to say at what precise point the one ends and the other begins. This is beyond question a fibroid change involving at the same time the pericardium and the capillaries. *f*, condensed fat; the rings are formed by the capsules of the oil-cells, which are less discrete and not so nearly circular as normal.

FIG. 45.—INFLAMMATION CAUSING CONDENSATION OF THE FAT LAYER OF THE HEART. (× 60.)

From the same section as Fig. 43. *p*, thickened and infiltrated pericardium; *c*, a capillary, and *v*, a larger-sized vessel which was curved so that it has been cut both longitudinally and across its calibre; both vessels are thickened. *f*, fat, which is condensed and changed by inflammation so that the rings are all small, ill defined, and crowded together, presenting a marked contrast in appearance to the fat in Figs. 44 and 1. *i*, an area of round-cell infiltration beneath the pericardium,—one stage of the formation of morbid fibrous tissue. Figs. 1, 44, 45 present three different conditions of heart-fat. The first is healthy, the second diseased, and the third very greatly diseased.

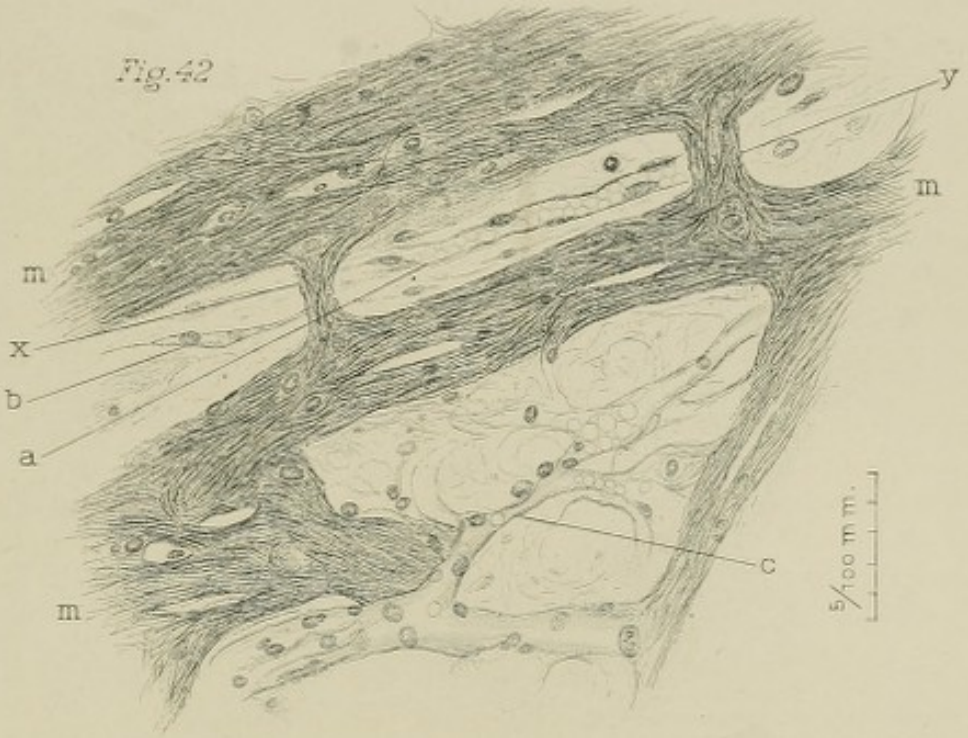


Fig. 42
y
m
m
x
b
a
c
m
5/100 m m.

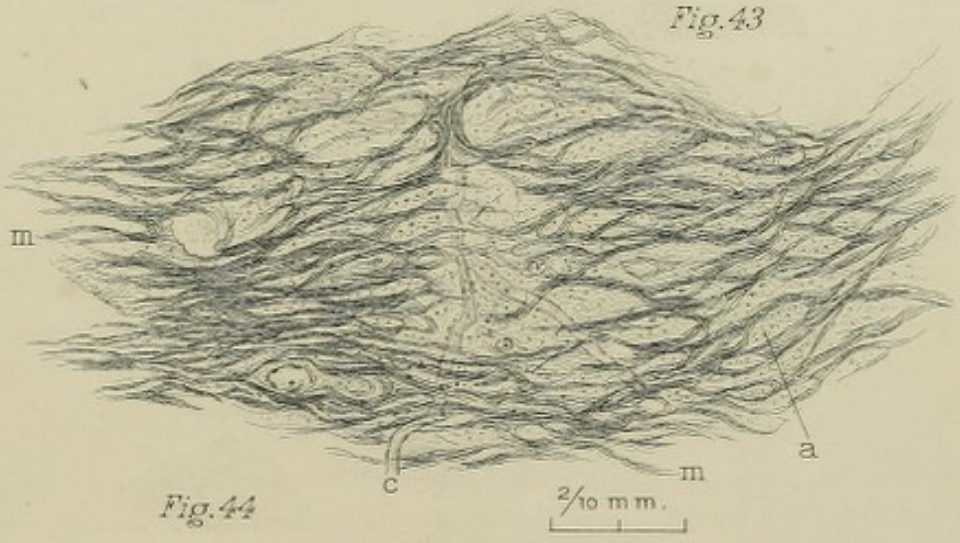


Fig. 43
m
a
c
m
2/10 m m.

Fig. 44

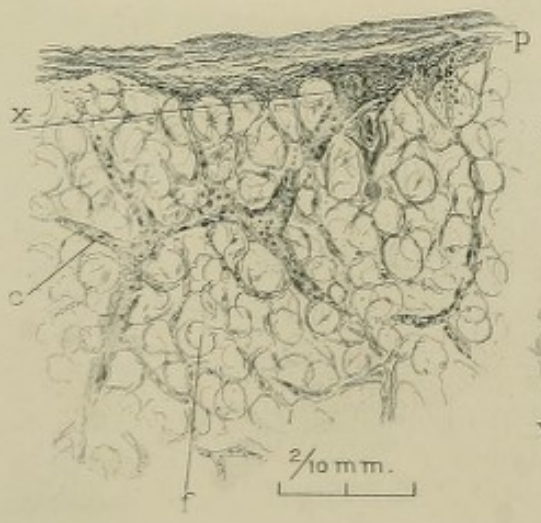
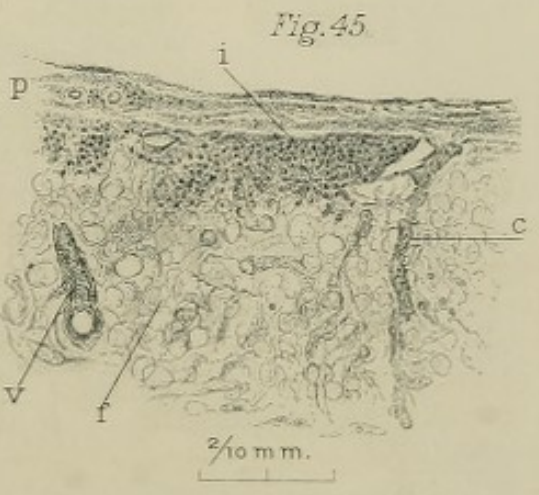

p
x
c
f
2/10 m m.

Fig. 45


i
p
c
v
f
2/10 m m.

should be examined, as it shows healthy heart-fat. It and Fig. 44 are from the same heart.

Disease of the fat layer of the heart is also shown by Figs. 46 and 47. The first of these represents a section through the entire thickness of the ventricular wall, and shows how the natural relative proportion of the various parts is changed. Instead of the fat being a thin layer upon the surface, its thickness is as great as and in places even greater than that of the muscle. Where they join, fat and muscle are much commingled, shreds of muscle running out into the fatty substance. Fig. 47, which is an enlarged view of *e*, Fig. 46, demonstrates that the growth of the fat takes place at the expense of the muscle, for the fat can be seen insinuating itself into the muscular tissue, rending the fibres and fibrils apart and destroying them. The appearances presented are such as to put it beyond doubt that the process of fatty infiltration is very injurious to the efficiency of the heart.

In the description of the changes which take place in the fat layer of the heart, it has been pointed out that the fibrous tissue growth plays an important part. A very different phase of cardiac fibrosis is shown by Fig. 52. The pericardium is greatly thickened, and its tissue contains many nuclei. The pericardial sac was obliterated by inflammatory adhesion. From the pericardium bands of new fibrous tissue extend into the substance of the heart. The effect produced is like that of water flowing in a stony brook, the fibrous bands being the water, and the muscular fibres which were cut across, the stones. When water flows among stones it finds its way where it can, in little streamlets resembling the bands of fibrous tissue extending inward from the pericardium. In a natural condition the muscular fibres of which the heart is almost entirely composed lie adjacent to one another, separated only by a very small amount of fibrous tissue. The condition represented, therefore, is very morbid, and the heart, although it was of about twice the natural size and had during life a heaving and forcible impulse, must have been a very inefficient pump. The question of the true meaning of enlargement or, as it is named, hypertrophy of the heart is most important, but it is discussed elsewhere (page 84). In Fig. 52 the muscular fibres appear to be completely solid, and in this respect they are in strong contrast with the disease next to be discussed.

That the muscular fibres of the heart are sometimes partially hollow is well known, and the disease has been called vacuolation. Some

time ago I published an essay upon the subject, in which it was asserted to be due to cystic degeneration.*

Figs. 48, 49, 50, and 51 represent variously hollowed-out muscular fibres. It has already been shown (page 65) that the fibres in the healthy human heart are penetrated by capillaries, and are not, therefore, as is commonly supposed, mere solid rods. Fig. 48 is a drawing under low amplification of a portion of a papillary muscle of the left ventricle from the heart of a man fifty-seven years old who died of Bright's disease. It is seen that most of the muscular fibres are hollowed out to a greater or less degree, and there is some increase of the intermuscular fibrous tissue. The contrast of these hollow fibres with the solid ones shown in Fig. 52 is striking. Fig. 49 represents a few of the fibres included in Fig. 48, more highly magnified to show the details of their structure. The destructive process, in its extreme development, removes the whole of the muscular substance from the centre of the fibre, leaving only thin outer walls.

A curious feature is that the nuclei often lie loosely in the cavities without attachment to the remaining tissue,—a condition very different from natural. The disease does not always show destruction of the entire central portion of the fibres, but sometimes eats them out irregularly, producing several smaller holes in different parts of the fibres. The varieties of appearance thus produced are very great, and the partitions separating the cavities are sometimes quite thick, and again thin and almost membranaceous. They may be incomplete, in which case they form shelf-like projections partially dividing the cavities. Fig. 50 is a longitudinal view of a fibre from the same heart as Fig. 49, and shows the hollowing of the central portion and four nuclei lying loosely in this cavity. The solid walls remaining are in places so far degenerated that the cross-striæ are indistinguishable, but in others they are distinct. The central cavity is subdivided by partitions at two or three places, and it contains amorphous material which is of varying degrees of density. At one spot the partitions are of such a form as to produce the effect of a circular opening, the appearance of which suggests the question whether it is a dilated capillary passing into or through the fibre. Fig. 51 represents fibres in transverse section from the heart of a woman forty years old who died of organic heart disease. The appearance is somewhat similar to

* Cystic Degeneration of the Muscular Fibres of the Heart, by Arthur V. Meigs, Transactions of the College of Physicians of Philadelphia, 1892, and The American Journal of the Medical Sciences, May, 1892.

FIG. 46.—FATTY INFILTRATION OF THE HEART. (× 3.)

From an elderly woman who died of dysentery and Bright's disease. The section includes the entire thickness of the left ventricle. *f* is the pericardium and *g* the endocardium; *b* and *b* are the cut edges. It is striking how thick the fat layer is, and, on the contrary, how thin the muscle, which has diminished owing to disease. *e* is a small vessel, and around it the fat has infiltrated the muscle so that it is shredded out and torn, appearing in the drawing as lines. *e* and the region around it are shown more highly magnified in Fig. 47.

FIG. 47.—FATTY INFILTRATION OF THE HEART. (× 50.)

Enlarged view of the region *e* in Fig. 46. *e* is here also the small arteriole; *v*, a vein filled with red and white blood-corpuscles; *f* is fat; *h* is muscular fibre. The drawing shows that the muscle is being destroyed by the growth of the fat, the oil-globules (circles as seen in cross-section) forcing themselves into the muscle and tearing the fibres and fibrils to pieces.

FIG. 46.

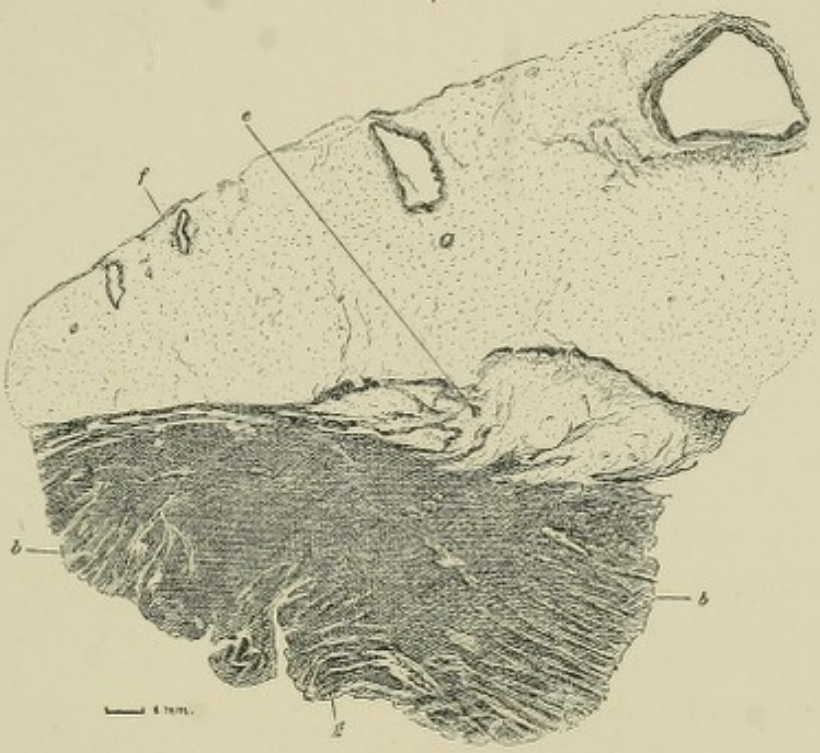


FIG. 47.

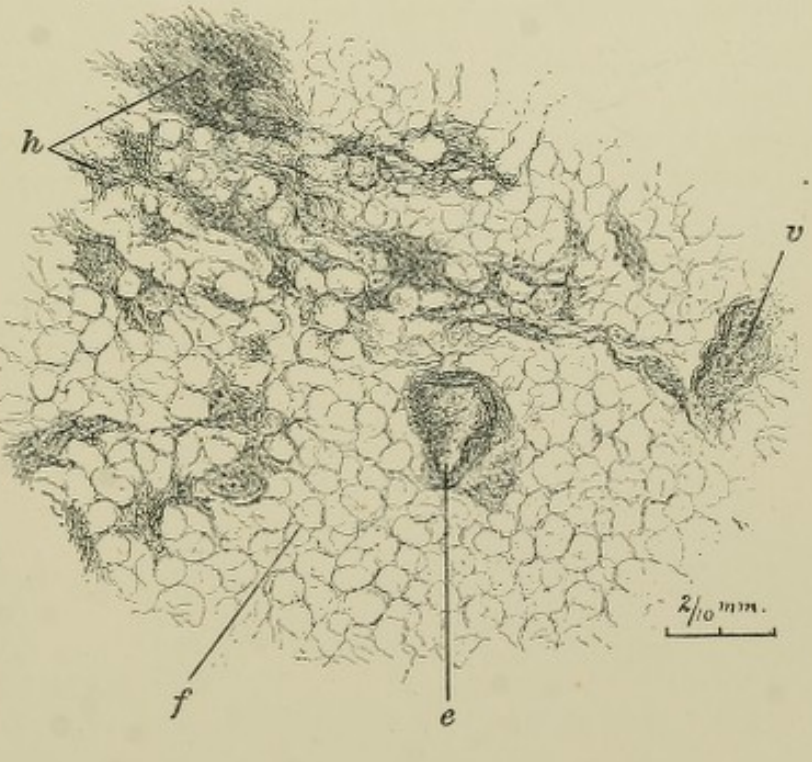


FIG. 48.—CYSTIC DEGENERATION OF THE MUSCULAR FIBRES OF THE HEART. (× 60.)

Section of a papillary muscle of the left ventricle, including a portion of the endocardium; from a man fifty-seven years of age who died of Bright's disease. *a*, *b*, *c*, and *d* are cystic fibres correspondingly lettered in Fig. 49. The drawing shows that most of the fibres are hollowed out, some more and some less. If they are compared with those in Fig. 52, which are solid, the contrast becomes striking.

FIG. 49.—CYSTIC DEGENERATION OF THE MUSCULAR FIBRES OF THE HEART. (× 340.)

An enlarged view of muscular fibres from the same section as Fig. 48. *a*, *b*, *c*, and *d* are fibres correspondingly lettered in Fig. 48. *a* is a large fibre in which the muscle nucleus lies free in a cavity. A portion of this fibre is divided into several smaller cavities which contain a little amorphous débris. *b* denotes two closely approximated fibres, or a twin fibre; there are large central cavities with shadowy threads of muscular tissue, which form partitions and shelves dividing or partly dividing the spaces into several cavities. The external rings of muscular tissue remaining constitute only a small proportion of the whole bulk of the fibre. At the point of junction of the two fibres the muscular tissue is fused so that there appears to be only a single wall. *c* has a large cavity eccentrically placed, and the muscular wall is still quite thick. *d* is eaten out into various irregular cavities; *e* and *f* are fibres still solid; they show that the muscular substance is arranged in a radiant striated manner. The nucleus of *e* is of very irregular shape.

FIG. 50.—CYSTIC DEGENERATION OF THE MUSCULAR FIBRES OF THE HEART. (× 340.)

A fibre cut longitudinally; from the same tissue as Figs. 48 and 49. Throughout the whole length of the portion included in the drawing the fibre is hollowed out in the centre, so that it forms a hollow cylinder whose cavity is divided by partitions. Within the cavity are four nuclei lying loosely in amorphous material, which is of varying density. The muscular tissue still left and forming the walls of the cylinder is in places in so good a state of preservation that the cross-striæ are distinct, while in others they have disappeared.

FIG. 51.—CYSTIC DEGENERATION OF THE MUSCULAR FIBRES OF THE HEART. (× 340.)

Transverse sections of muscle fibres from the anterior portion of the heart, near the pericardial covering; from a woman forty years old who died of organic disease of the heart. The process is seen at an earlier stage than in the preceding figures. There are many small cavities, and fine thread-like divisions between some of them. *b* denotes two fibres or a twin fibre, and in the portion to the left some of the spaces are strikingly like capillaries. *a* is a fibre partly solid and partly eaten away.

FIG. 52.—FIBROID HEART. (× 60.)

Section of the anterior portion of the left ventricle, including the pericardium; from a man sixty years old who died of gout and Bright's disease. *x* to *y* is the pericardium, which is enormously thickened and consists of dense fibrous tissue containing many nuclei. From the pericardium and continuous with it are bands of fibrous tissue (*b*) which pass in among the muscular fibres (*m*): the appearance is like that of water flowing among stones in a brook. The muscular fibres (*m*) which have been cut across are almost all separated by an interval instead of touching or nearly touching one another as is natural, and the space between is filled by fibrous tissue (*f*) which is rich in nuclei. The muscular fibres themselves are all solid. The appearances suggest that a new and rapidly growing fibrous material was fast extinguishing the muscular tissue.

Fig. 49

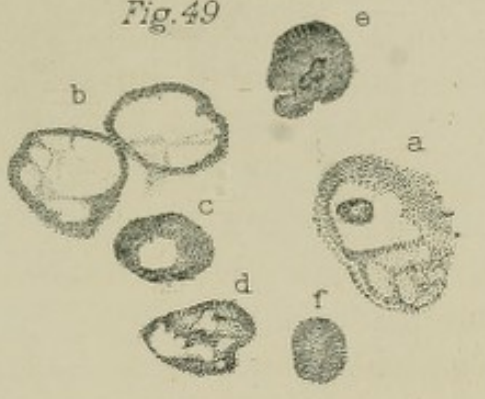


Fig. 48

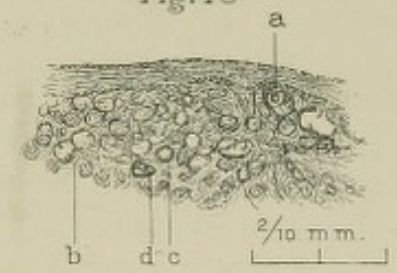


Fig. 50

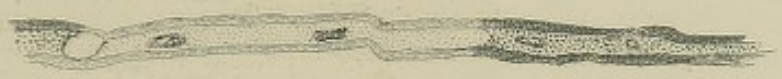
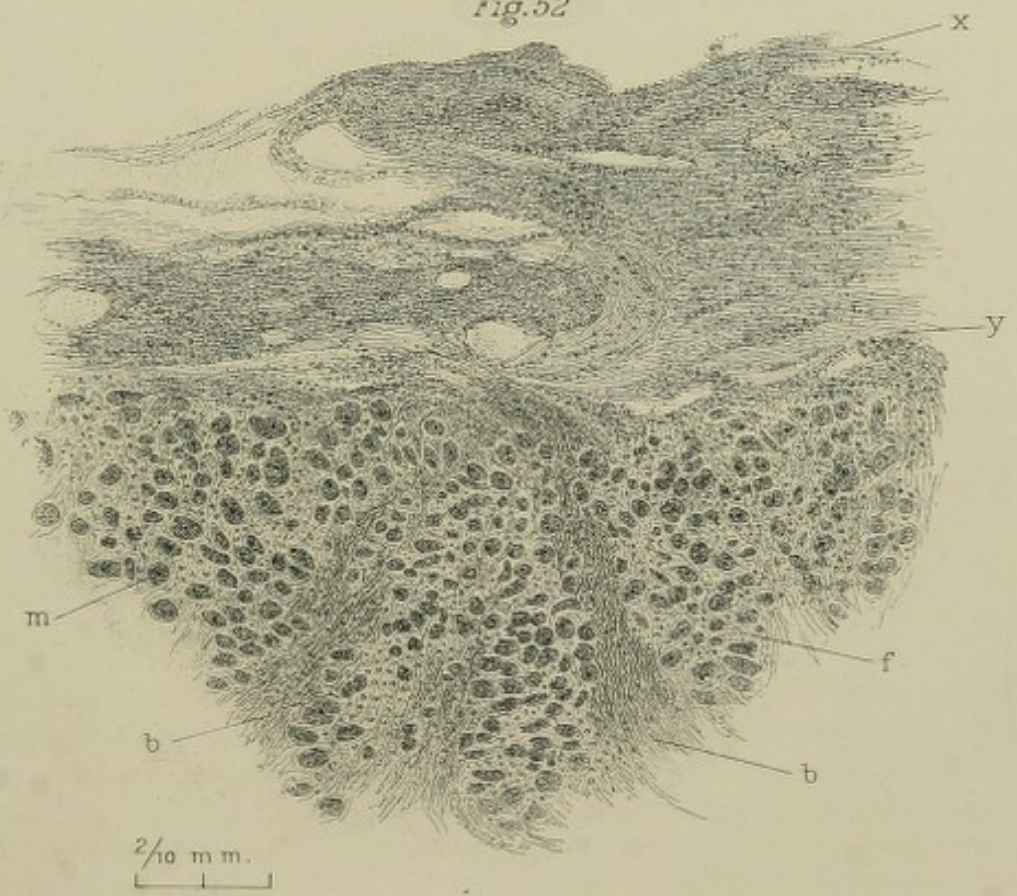


Fig. 51

Fig. 52



that of Fig. 49, but the disease is less advanced. There are numerous small spaces, but there is still a good deal of muscular tissue remaining. These fibres look like old worm-eaten wood. The material separating some of the cavities (*b*) is a thin but distinct membrane, looking exactly like the endothelium which forms the walls of capillaries. The cavities in muscular fibres do not give the impression that during life they were empty, or even that they contained only a clear liquid, but generally there is within them more or less material, without distinguishable structure, which is represented in the drawings by dots. Hollow fibres are found in all parts of the heart, but they occur more frequently near the serous surfaces. In fibroid hearts they are common, but generally absent from the most fibroid portions.

It is not possible at present to predict from any clinical manifestations in what cases hollowing of the muscular fibres of the heart will be found. The examination of many sections has demonstrated the condition to be absent in cases clinically recognized as brain syphilis, sarcoma, general miliary tuberculosis, Bright's disease, pulmonary phthisis, typhoid fever, pneumonia, dysentery, epithelioma of the bowel, and aneurism; and, on the other hand, to be present in organic heart disease, Bright's disease, typhoid fever, ulcerative endocarditis, and in young infants that had died of wasting. Thus it is seen that in cases of the same disease it is sometimes present and sometimes absent. In foundlings dead of wasting during the early months of life, the muscular fibres are hollowed in some instances and not in others. In a child of ten who died of amyloid disease of the heart, lungs, liver, spleen, and kidneys, I found extreme hollowing of the muscular fibres of the heart. Some of the fibres in this case, when seen in longitudinal section, presented small, bulbous-looking swellings at points where they were hollow, making it appear as if some distending process had occurred at the points where the hollowing existed.

The disease has been called vacuolation and hyaloid degeneration, and I have attributed it to cystic degeneration. The fact that the fibres are penetrated by capillaries and are not therefore solid bodies, together with the appearance of the cavities and the nature of their contents (see page 75, Fig. 58), leads inevitably to the conclusion that the capillaries have some connection with the production of the disease. The material within the cavities is amorphous or granular, or there is yellowish pigment in irregularly shaped flakes, looking as if suspended in a liquid. The appearances described are those of partially destroyed blood, and if the contents of the cavities

are derived from the blood there is no escape from the conclusion that they are of the nature of cysts. In Fig. 58 there are bodies in one of the hollow fibres which look like partially degenerated blood-corpuscles. If the cavities contain blood, then they are cysts or aneurisms according as they had still a connection with the blood-stream or were cut off from it. The appearance of the cavities indicates that in most instances they were closed sacs and were therefore true retention cysts, although in such a cavity as one of those in Fig. 58 there may have been still an opening connecting the cavity with the blood-channels. Figs. 53 to 58 exhibit hollowing of the muscular fibres, attenuation and degeneration of them, and the ramifications of the capillaries of the heart. Fig. 53 shows a phase of hollowing of the fibres of which I have not seen any other example. The muscle is somewhat granular, but a few of the cross-markings can still be distinguished. The two fibres are hollow, and this is very distinctly to be seen, as, although cut longitudinally, they were so bent that the ends were cut across. These cut ends appear as rings of muscular substance, in which the fibrillæ can be distinctly seen surrounding cavities. In the section from which the drawing was made the hollowing has proceeded to such a degree that it is in some instances impossible to decide whether a given hollow cylinder is a blood-vessel or a muscular fibre. There can be no doubt that those represented in the drawing are hollow muscular fibres, for the ring of tissue is easily recognized as muscular, but in others which are still more degenerated a distinction cannot be made. Figs. 54, 55, 56, and 57 are views of transverse and longitudinal sections of fibres from the left auricle of a youth of seventeen who died of organic heart disease. There was complete obliteration of the pericardial sac; the heart was greatly enlarged, and the left auricle had undergone fibroid change to such a degree that it was difficult with the naked eye to distinguish any muscular tissue in it. The color of the auricle was a light grayish brown, instead of red. The fibres are not hollowed, as they sometimes are. These fibres present a parallel in miniature to what occasionally takes place in the heart itself. In a natural condition the muscular fibres of the heart are placed close together, generally touching one another; disease changes this, and by the growth of fibrous tissue or by other cause they are forced apart. In healthy fibres the fibrillæ also are so close together that there are no intervals between them, and it is only by careful study with the microscope that the division into fibrillæ can be distinguished.

FIG. 53.—HOLLOW MUSCULAR FIBRES OF THE HEART. (× 240.)

From a woman of thirty years who died of Bright's disease : there was cardiac fibrosis, and in places the muscular fibres were very much attenuated. Three fibres are included, cut somewhat in their length, but they were so turned that their ends, two of which are hollow, are seen in cross-section. There is a muscle nucleus in the upper fibre. The cross-markings can be distinguished, but the muscular substance is somewhat granular. Around the hollow ends the subdivision into fibrillæ shows very distinctly.

FIG. 54.—ATTENUATED AND DEGENERATED MUSCULAR FIBRES OF THE HEART. (× 240.)

A section of the left auricle from a youth seventeen years old who died of organic disease of the heart : the fibres are cut transversely. Figs. 55, 56, and 57 are from the same section. There are numerous large open spaces in the fibres, and the fibrillæ appear as dots with space between. The small delicate rings between the muscular fibres are capillaries. *a*, *b*, and *c* are the fibres represented more highly magnified in Fig. 55.

FIG. 55.—ATTENUATED AND DEGENERATED MUSCULAR FIBRES OF THE HEART. (× 400.)

The fibres *a*, *b*, and *c* from Fig. 54, more highly magnified ; correspondingly lettered. The large space in *b* is sharply outlined, and its appearance strongly suggests that it has a wall of endothelium ; in *a* and *c* the spaces are somewhat irregular in shape. The appearance of the fibres is peculiar ; more than half of the muscular substance has disappeared, and therefore the fibrillæ which remain appear as dots, distinctly separated from one another. Between the dots, however, there are fine threads, so that the appearance is like that of an irregular cobweb.

FIG. 56.—ATTENUATED AND DEGENERATED HEART MUSCLE WITH CAPILLARIES WITHIN THE FIBRES. (× 400.)

From the same section as Figs. 54, 55, and 57 : fibres cut longitudinally. The muscle looks much less solid than usual, and the fibrillæ are separated from one another. The isolation of the fibrillæ causes the cross-striæ to be unusually distinct. There is a cavity at either end of the nucleus *x*, and the nucleus looks as if it had been indented by a capillary tube which had pressed against it in passing obliquely through the fibre. *y* is a nucleus which, in connection with the opening above it, looks still more as if a capillary had passed obliquely through the fibre, indenting the side of the nucleus in its course.

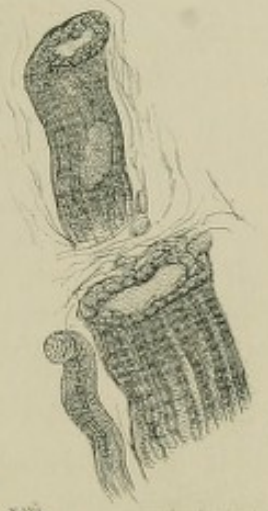
FIG. 57.—CAPILLARIES ENTERING MUSCULAR FIBRES AND RAMIFYING AMONG THEM. (× 240.)

From the same section as Figs. 54, 55, and 56, but less highly magnified than the last, showing the ramifications of the capillaries among the muscular fibres and how they appear also to pass into them. The tenuity of the fibres, the way the fibrillæ tend to stand apart, and the great distinctness of the cross-markings are beautifully shown.

FIG. 58.—CYSTIC DEGENERATION OF THE MUSCULAR FIBRES OF THE HEART. (× 240.)

From a negro man of thirty years who died of organic disease of the heart. *m* denotes portions of muscular fibres which are somewhat granular in appearance ; other fibres are hollowed out and changed so that if they were by themselves it would be impossible to recognize them as muscle. *e* and *f* denote hollow fibres whose contents appear like disintegrated blood, being composed of granular material and circular or partly circular bodies like degenerated red blood-corpuscles. *c* is a fibre with thin fibrous-looking walls and a large central cavity partly filled with débris. At the lower end of *c* the semicircle formed by the inturning of the walls appears to form a partition in the cavity ; above is an elliptical opening looking like a capillary cut across. The conditions suggest a minute aneurism, the blood having entered by the elliptical opening and torn away the whole of the centre of the fibre to form a cavity for itself.

Fig. 53



5/100 m.m.

Fig. 54

Fig. 55

5/100 m.m.

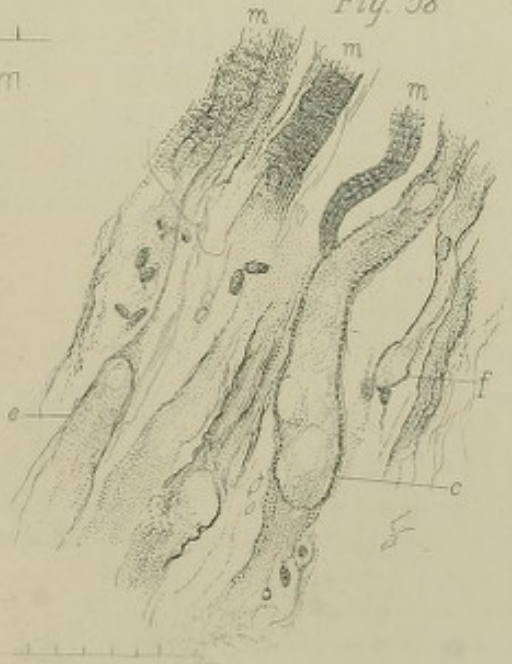
Fig. 56

5/100 m.m.

Fig 57

5/100 m.m.

Fig. 58



5/100 m.m.

In the drawings the fibrillæ are seen to be separated from one another by distinct intervals both in cross-section and in longitudinal section, and thus the parallel is complete. Fig. 54 represents a group of muscular fibres in cross-section which are evidently greatly diseased. Their average size is much less than natural, and, instead of being almost solid, they are of open structure, the fibrillæ being separated from one another. The separation of the fibrillæ varies much in different fibres. There are no hollow fibres to be seen like those in Fig. 58. A few capillaries are visible in the interspaces, and in several of the fibres are circular openings which probably are dilated capillaries. Fig. 55 represents three fibres included in Fig. 54, more highly magnified to show details of the structure. These are the capillaries in the fibres, and in one of them (*b*) the endothelial wall is visible in the preparation, but this feature is imperfectly shown. The space between the fibrillæ does not appear to be empty, but contains fine cobweb-like threads which look as if they ran from one fibrilla to another. This, too, the drawing fails to show exactly as it is seen with the microscope. Fig. 56 is a longitudinal view of fibres from the same section as Figs. 54 and 55. It shows great tenuity of the fibres, which are of less than average width, and the fibrillæ are separated in an unnatural way. The cross-striæ are much more distinctly seen than is usual, and it may be that this is a result of disease, but it is much more likely that it is due to the free passage of light through the spaces between the fibrillæ, admitting of better illumination than can be had in healthy muscle, in which the fibrillæ are in contact. The spaces between the fibres are filled with fine fibrous tissue. The muscle-nuclei have spaces at both their ends, as is usual in all heart-muscle except that of very young infants, but in two of those here depicted (*x* and *y*) the shape of the nuclei and of the spaces in which they lie is such as to suggest that capillaries passed through the fibres, indenting the nuclei upon the side. In one of the fibres (*y*) this appearance is very distinct, but it is only moderately well shown by the drawing. These spaces at the poles of the nuclei, which are present in some degree in almost all pathological hearts, are commonly attributed to what has been named brown atrophy. The nature of the amorphous and pigmented material and the fact that the fibres are penetrated by capillaries make it probable that the material is derived from the blood, and that the spaces have some connection with the circulation. Fig. 57 is a group of fibres from the same section as Fig. 56, less highly magnified, and it shows

the separation of the fibrillæ, which are woven in and out in the fibres like the strands of a plaited rope. The cross-striæ are very distinct, and the spaces between the fibres are filled with fibrous tissue, which is present in unnaturally great amount. The special feature, however, of this illustration is the exhibition it makes of the ramifications of the capillaries. Owing to the tenuity of the muscle and the separation of the fibrillæ permitting of the passage of light with unusual freedom, these can be seen with a distinctness that I have not noticed in any other tissue. The capillaries as seen with the microscope appear to pass directly into the fibres, and this effect is well reproduced by the drawing. The four sections last described illustrate a very curious form of fibroid disease of the heart. The heart from which the sections were taken was inflamed, for there was great increase of the intermuscular nuclei; it was generally fibroid and greatly hypertrophied, and the pericardium was adherent. In addition to all this there was such extensive fibrosis of the auricles that they looked more like connective tissue than like muscle, for the tissue was grayish-white instead of red like healthy muscle. Microscopical examination demonstrated extensive disease of the endocardium and of the pericardium, and the auricular walls were composed of thickened endocardium and pericardium with only a thin stratum of muscle between. It seems impossible that the auricles could have had any contractile power left. The marked peculiarity of the fibroid disease in the case lies in the condition of this thin remnant of the auricular muscular tissue.

In Figs. 54, 55, 56, and 57 there is no hollowing out of the muscular fibres, nor are they granular or fatty. The peculiarity consists in their attenuation and in the separation both of them and of the fibrillæ from one another. The substance that filled the spaces between the fibres and between the fibrillæ must have been something of the nature of fibrous tissue. The condition is one I have never seen developed to an equal extent in any other case. Fig. 58 is heart-muscle from a man thirty years old who died of organic heart disease. There are parts of fibres included which can still be recognized as muscular tissue, although the cross-striæ do not show very well and it is somewhat granular. Most of the fibres, however, are so diseased as to be past recognition, being composed of large central cavities with thin fibrous walls. These walls, unlike those of the fibre shown by Fig. 50, do not look in the least like muscular tissue, but are purely fibrous in their composition. The effect is as if the whole of the muscular

substance had been removed, leaving behind it an empty shell. Some of the fibres contain within their cavities circular bodies resembling partially disintegrated blood-corpuscles. In the drawing this peculiarity is somewhat exaggerated, for the circular bodies can be seen with the microscope only after careful study. At positions where the fibres are most hollow they are swollen, producing bulbous enlargements; this is seen in several of the fibres. Such swelling could result only from distention of the shell of the fibre by the accumulation of some material within the cavity. At the upper end of one fibre (*c*) which is completely hollowed and presents a distended appearance, there is an elliptical opening which looks as if a capillary, cut obliquely, had entered the cavity. Taken together, the appearances of these fibres lend strong support to the view that the hollowing of the muscular fibres is a true cystic degeneration and that the cysts originate from the capillaries within the fibres. Figs. 53 to 58, all included upon the same plate, make a good demonstration of the extreme variability in size of the muscular fibres of the heart. One of the fibres in Fig. 53 is the largest of any shown. In comparing them it must be kept in mind that Figs. 55 and 56 are almost twice as much magnified as the other four. Extreme tenuity of the fibres and reduction in their size are among the most common and striking peculiarities of long-standing disease of the heart. These changes seem to belong especially to those cases in which there was inflammatory disease for a long time before death. Another strange and at present inexplicable feature is that in cases of fibrosis the fibres are sometimes hollow, and again they are more solid in appearance than in histological tissue.

Figs. 59 to 62 illustrate cystic disease of the heart. A full account of the case, which was one of cystic disease of the heart, liver, spleen, and kidneys, has already been published,* but with very inadequate illustrations. Fig. 59 shows many cavities. These are of different sizes and are variously placed, sometimes singly, at other times close together. In some places only thin membranous walls separate one cavity from another, and in others two or more cavities are joined, being only partially separated by broken or incomplete partitions. Examination of the section with greater amplification shows that the heart is fibroid, the fibrous increase being greatest near the endo-

* Cystic Degeneration of the Heart, Spleen, Liver, and Kidneys, by Arthur V. Meigs, Journal of Anatomy and Physiology, vol. xxvii.

cardium and around the papillary muscles. The fibres are pushed apart, and there is increase of the intermuscular nuclei, showing that there had been inflammation. The cysts are usually surrounded by muscular tissue, there being no differentiated cyst-wall. In places, however, there is a very distinct cyst-wall quite different in its constitution from the muscular tissue. This consists of a fine structureless or fibrous membrane, the so-called basement membrane, and in it are flattened nuclei, like the common endothelial nuclei of capillaries and of the intima of arteries. A differentiated cyst-wall is more often found in small cysts than in the larger ones; and if there is any cyst-wall in those of large size it has generally been broken, thus giving the impression that the membranous walls had been torn through and destroyed as the cavities grew larger from the increase of the quantity of liquid contents. In places there is marked condensation of the muscular tissue around the cysts, and here and there portions of cyst-contents, consisting of structureless material, have been included. The amount of solid material within the cysts must have been very small,—a few flocculi in the liquid. It is remarkable that there should have been in the same case cystic degeneration of four of the most important organs of the body, and it is improbable that the cysts had different modes of origin. The cause that produced them in one organ produced them in all. Cysts are classified in two great divisions,—true cysts and pseudo-cysts, or spurious cysts. The latter are those which arise in the substance of the organs or tissues owing to hemorrhage or disintegration or other pathological process, while true cysts have their origin in the abnormal dilatation of a pre-existing tubule or cavity. It does not seem likely that the cavities shown in the illustrations are spurious cysts, for such an assumption is negatived both by their appearance and by the fact that true cysts having precisely the appearances of these are well known to occur in the kidneys and in the liver. It is probable that the cavities in the four organs had a common mode of origin; but, so far as the spleen and the heart are concerned, except the blood-vessels and the lymphatics there are neither pre-existing tubules nor cavities which could undergo abnormal dilatation. The cavities are not pseudo-cysts, and, this being the case, they must be true cysts, originating in blood-vessels or lymphatics. Of diseases of lymphatics there is as yet very little known, but cystic dilatations of blood-vessels resulting in the production of aneurism, varix, and capillary aneurism are among the most common of pathological processes.

FIG. 59.—CYSTIC DEGENERATION OF THE HEART. (× 7.)

From a man of seventy-seven years who died of cystic disease of the heart, liver, spleen, and kidneys. The cysts vary in size and are irregular in shape; some of them are separated only by thin membranous-looking partitions. The walls of some are in parts condensed and thicker than the tissue elsewhere. *c* is a cyst which with the surrounding tissue is represented more highly magnified in Fig. 60. Figs. 60 and 61 are from the same section, and Fig. 62 is from another section of the same tissue.

FIG. 60.—CYSTIC DEGENERATION OF THE HEART. (× 50.)

An enlarged view of the region *c* in Fig. 59. The cyst is a large opening which to the left has no apparent outlet, while to the right it is continued into a long narrow channel. *e* is a delicate membrane-like endothelium, which is to be seen upon both sides of the narrow channel and to some extent in the larger portion of the cyst. In this membrane are a number of bead-like cells which resemble endothelium. *x* is the centre of the region represented more highly magnified by Fig. 61.

FIG. 61.—CYSTIC DEGENERATION OF THE HEART. (× 250.)

The region *x* in Fig. 60, more highly magnified. *y* corresponds in position with the end of the leader *x* in Fig. 60. *m*, muscular tissue, some upon both sides of the channel being included. It is degenerated, in places the cross-markings being visible and again having disappeared. *e* is the endothelium, and it is well defined upon both sides of the channel and contains a number of nuclei. At *a* is a nucleus which is histologically typical; it is enclosed by the endothelial plate, which has split into two layers to surround it like a frame.

FIG. 62.—CYSTIC DEGENERATION OF THE HEART. (× 50.)

From another section of the same tissue as the preceding, showing the breaking down of the substance of the heart. Above is a cyst which is nearly circular and does not seem to be connected with any other. Below is an irregularly shaped and imperfectly divided collection of cysts with shreds and fibres of degenerated muscular tissue to form such walls as exist to separate one cavity from another.

Fig. 59.

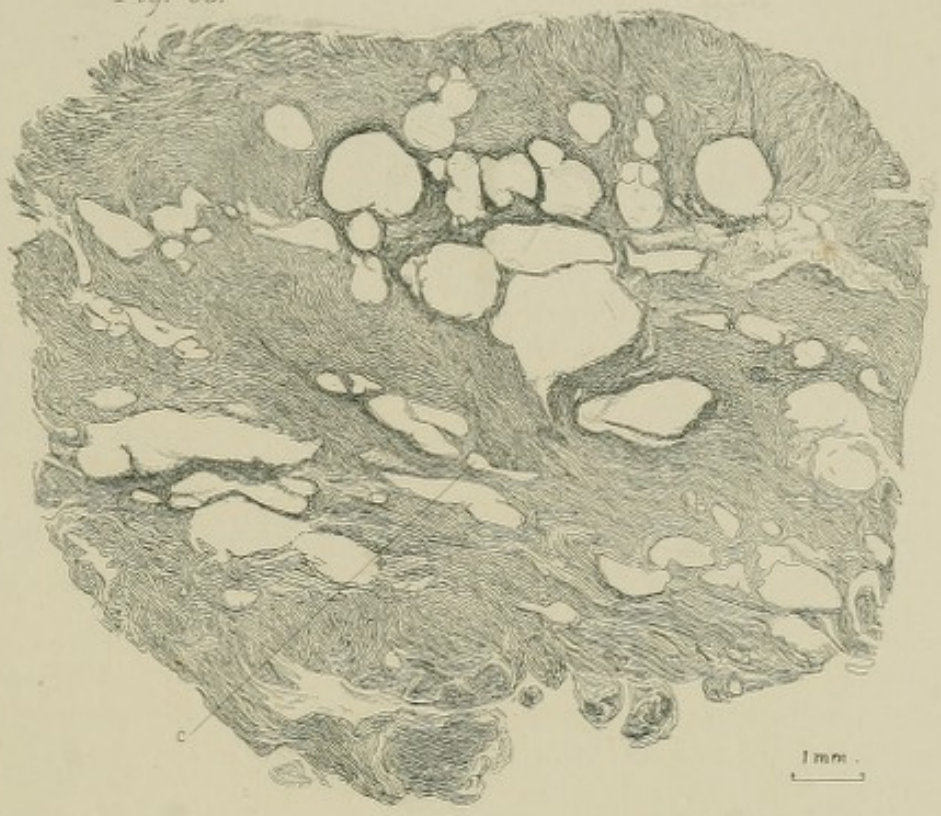
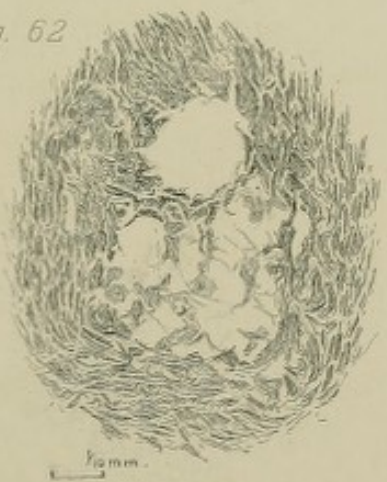


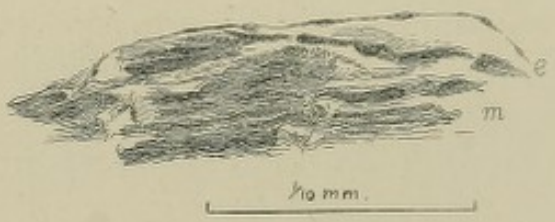
Fig. 60

Fig. 61

Fig. 62



y



Figs. 60 and 61 represent, more highly magnified, one of the cysts in Fig. 59. The larger cavity in Fig. 60 is prolonged into a narrow channel, and both the cavity and the channel are partly lined with a membrane which is in every respect identical with the endothelium which forms the walls of capillaries. Fig. 61 is a portion of the channel still more magnified, and it shows the membranous endothelial lining and the flattened nuclei peculiar to that sort of tissue (see description of plate). Fig. 62 is from another section of the same tissue, and it shows cavities with shreds of tissue irregularly separating them,—an early stage of the cyst-formation. These partitions, when examined with greater amplification, will be seen to be formed of muscular tissue and portions of fibrous material. The effect is as if a liquid had accumulated and had increased in quantity, separating and tearing the muscular fibres apart and destroying them. The parallel with what takes place upon a large scale in arterial aneurism is very close. In aneurism the distending force is so great that even so rigid a barrier as the bony spinal column must yield if it happens to be in the way. It seems as if there must be some connection between the hollowing of the muscular fibres which has been described and cystic disease.

Study of the gross post-mortem appearances with the clinical histories of eighty-nine cases and microscopical examination of the hearts lead to a number of interesting observations. The heart in the earlier periods of life differs from the heart in old age; it changes gradually, but disease sometimes makes the young heart very like that of more advanced life. At an early embryological period no cross-striæ can be seen in the muscle cells, and even in young infants the striæ are not easy to distinguish and have not the appearance that they acquire during adult life. In youth the heart is of a closely knit texture, the muscular fibres being placed so close together that it is difficult to distinguish an interval between them, and there is scarcely any fibrous tissue to be seen except in the spaces where the blood-vessels lie. As life advances, fibrous tissue accumulates and the fibres become separated. To a certain extent this change must be considered as histological and natural to the advance of life, but, as has been shown in the preceding pages, it is often the result of disease. It has been said that that curious form of degeneration, hollowing of the muscular fibres, may occur in very early life. It has been found in infants a few months old, and in children of from nine to twelve years, and sometimes the fibres are swollen and bulge at the points of

greatest hollowing, just as they have been shown to do in older persons. It has already been stated that hollowing of the muscular fibres sometimes occurs to such a degree and in such form that it may be impossible with certainty to distinguish whether a given hollow cylinder in a section of the heart is a muscular fibre or a blood-vessel. The hollowing of the muscular fibres might be thought to be a result of fatty degeneration, but testing with osmic acid shows that such is not the case; besides which, the hollowed fibres do not look like fatty degeneration. Hollowing of the fibres, fibrosis, and increase of the intermuscular nuclei often exist together in the same case. An important observation is that which was made in connection with the capillary nuclei, which appear to enlarge so as to obstruct if not shut off the capillaries. In sharp contrast with the hollowing of muscular fibres is the unusually solid appearance they sometimes present, even in hearts that are very fibroid and diseased. (Fig. 52.) Condensation of the fat until hardly any fat cells are left and it becomes a fibrous tissue containing a greatly increased number of capillaries is one of the commonest changes in hearts that have been long subjected to chronic inflammation.

The shredding apart of the muscular fibres and the fact that they become so distorted as to run at right angles to one another, and attenuated and narrow (Figs. 42 and 56), have already been mentioned. These conditions are very common in fibroid hearts and in those that have been subjected to long-standing inflammation: such organs must be very ineffective pumps. When a heart has been in a condition of chronic inflammation, one of the most striking changes that take place is the great increase of the number of intermuscular nuclei. This is one of the commonest appearances discovered in the hearts of those dead of chronic disease. Granular degeneration of muscular fibres is spoken of in pathological works as though it were one of the commonest and best known of diseases. In truth, however, it is generally very difficult to decide in a given section whether a certain indistinctness of the cross-striæ and a slight granular or powdery look of the fibres are really due to granular degeneration or only to faulty preparation of the section. Among the eighty-nine hearts of which I have sections, there is one in which granular degeneration has proceeded so far that the individual granules can be seen as blackish dots. Such an appearance is certainly pathological, and muscular fibre so affected must be inefficient in function. In the case of a child of twelve who died having amyloid degeneration of the liver and

kidneys, and in whom there had been long-standing organic disease of the heart, the pericardium was found adherent to such a degree as to have obliterated the pericardial sac. In the fibrous tissue over the heart, which was composed of the thickened pericardium and new growth which bound the two layers of the pericardium together, was material which resembled amyloid deposit. Amyloid disease of the heart is not described as being of frequent occurrence, but it is highly probable that if sought for it would be found to be much more common than is generally supposed. The heart has not been subjected to microscopical examination by any means so frequently as the liver and the kidneys. The condition which is described as brown atrophy of heart-muscle is so very common and is so universally considered in pathological treatises as one of the well-recognized forms of cardiac degeneration as to make it desirable that it should be as well understood as possible. So far as my own experience goes, in the microscopical examination of the heart there is always more or less of this so-called brown atrophy existing in the hearts of those who have reached adult life. If this observation be correct, it would seem to indicate that the condition may be one not always to be classified as a disease. There are differences between young and old hearts which are in their extremes of development as striking as the differences between health and disease. Brown atrophy is described by Ziegler, whose text-book on pathology is standard, as a condition in which the "fibres are smaller than normal and contain to a greater degree than usual small yellow pigment granules. These lie mostly at the poles of the nuclei, but are also scattered in the protoplasm of the cells." It is noticeable that Ziegler says the pigment granules are present to a greater degree than *usual*, which is as if he believes their presence to be normal. My own belief has been stated that, as the pigment is invariably present in adult hearts, some other explanation of its existence must be found than the assumption that it is always the result of disease.

Whether or not the nerves of the heart are commonly diseased, and what influence, if any, their condition has in the production of recognized complaints, are important questions which have occupied some attention. Nervous tissue is always difficult to study, as it is of very delicate structure, and for this reason, and because it has not yet been exhaustively examined, no very satisfactory conclusions are at present attainable. In no one of my sections from eighty-nine hearts is there included any portion of a ganglion or a single medullated

nerve fibre, while on the other hand there is hardly a section that does not include one or more non-medullated fibres. In the sections of the anterior portion of the heart, including the pericardium and the layer of fat, it is rare to find one that contains a blood-vessel without one or more nerve filaments. The nerves, as elsewhere, accompany the vessels, but these nerves are, so far as my experience goes, all of the non-medullated form. The structure of non-medullated nerves is so lacking in distinctive character that it is difficult to feel sure that any particular one is diseased or healthy. In appearance they are like bits of fibrous tissue, and it is impossible to decide that some slightly unusual appearance is not due to a fault in the preparation of the section. However, there are in my possession sections which have seemed to me to demonstrate disease of the nerves.

The condition called fragmentation, which has been described by more than one author,* and which consists in a separation of the muscular fibres transversely, is very common among persons who have died of heart disease. It has been supposed to be a giving way of the cement substance, and has been said by some to occur only in the death-agony. Neither of these views seems to be very well supported, and the likelihood is that fragmentation is a disease, but a true understanding of its origin and possible importance is as yet beyond our reach.

In order to grasp all that can be understood of heart disease, it is necessary to have as complete a knowledge as possible of the anatomy of the heart. The description, therefore, that has been given of the relations of the cardiac blood-vessels to one another and to the muscular tissue is important. There are at least two conditions in this connection which are peculiar. These are, first, that almost all the efferent vessels in the substance of the heart, even when they are of good size and are accompanying vessels to arterioles having three coats, are thin-walled and structurally identical with the smallest capillaries. There are, therefore, but few of the ordinary veins with three coats in the substance of the heart. The second anatomical peculiarity of importance is that the capillaries penetrate the muscular fibres, and do not simply ramify among them and surround them, as has been heretofore believed. It is difficult to refrain from speculation in regard to the effects of these two strange anatomical condi-

* Ueber die Fragmentation des Myocardium, Alessandro Tedeschi, Virchow's Archiv, 1892, Bd. cxxviii. Ss. 185–204.

tions which belong to the heart alone. It is not speculation, however, to say that the large efferent vessels which take the place of the small-sized veins which exist in other tissues must serve at least two purposes more than those of ordinary veins: they act as reservoirs to a greater extent than common veins, and they partake directly in the nutrition of the tissue. In all parts of the body the venæ comites are found after death to be larger than their companion arteries, but in the substance of the heart this peculiarity is greatly exaggerated. The efferent vessels, which might well be named venous capillaries, are many times larger than the arterioles by which they are accompanied, and therefore their capacity to serve as reservoirs must be vastly greater than that of ordinary veins, both because of their exceptionally great size, and because their thin walls can dilate much more, and more easily, than the thicker and comparatively rigid walls of common veins. It has been demonstrated by physiologists that the capillaries directly nourish the tissues by the transudation of blood-corpuscles through their walls and by osmosis of the fluid nutritious portion of the blood. The large efferent capillaries which in the heart replace the veins of other tissues are structurally identical with ordinary capillaries, and must therefore possess the same power to permit of transudation. As it is not conceivable that all the nutritious material has been abstracted from the blood before it reaches the venous capillaries, they must to some extent continue the function of nutrition, although it is principally performed by the ordinary capillaries. Besides their office of nutrition, blood-vessels effect the work of the removal of the waste products from the tissues. In the heart it would seem that the large venous capillaries, occupying the place ordinarily taken by veins, must afford the opportunity for waste material to enter the blood with greater ease and more completely than if there were veins as in other tissues. For veins, being relatively thick-walled, are supposed not to permit transudation.

No illustrations of valve-lesions, nor any extended discussion of valvular disease of the heart, have been included in this chapter, because the subject has been so exhaustively studied that it would not be possible to add much to what is known. The accumulation of facts in regard to the various distortions of the valves and the enlargement or contraction of the valve-openings which almost invariably accompanies the changes of the flaps is enormous.

Although the physical alterations of the heart-valves which are caused by disease are so well known, the effects of such changes are

not generally understood. It is almost certain that theory has run far beyond what is warranted by the facts, and that the laws of hydrodynamics have been forced into use in such a way as to lead to false deductions. Owing to the conditions of living beings, it has been impossible as yet to measure the various forces that govern the heart's action so as to make a comparison with the pumps made by men's hands. These work according to the laws of water- or steam-pressure, the size and strength of pipes, the action of mechanical valves, and other such things which can all be easily calculated to a nicety by an expert and the resultant effects predicted. An extended discussion of this subject belongs more properly to a subsequent part of this chapter (page 84), where it will be considered in connection with the characteristics of hypertrophy of the heart.

Fatty infiltration of the heart has commonly been considered to be rather a harmless condition. My illustrations show that such is not the case, for, in addition to the embarrassment of free movement which the presence of the fat necessarily entails, its growth takes place partially, at least, at the expense of the muscle. Sufficient evidence has not been collected to justify the positive assertion that the accumulation of fat upon the heart, when it becomes more than the thin layer that is usually found upon the hearts of all but very young persons, is necessarily a disease. When the layer of fat does become thick, the amount of muscle is sometimes proportionately diminished (Fig. 46), and, although it would be unwarrantable to say that this is invariably the case, the mode of growth of the fat makes it in the highest degree probable that a thick fat layer always morbidly interferes with the integrity of the muscle. Its very presence is obstructive, and its habit is to force itself into the cardiac septa and between the muscular fibres, in doing which it always destroys some of them. Besides this, the fat itself is frequently the seat of disease. Inflammation of the heart-fat and its condensation and conversion into morbid fibroid tissue are of frequent occurrence. This has been discussed and the appearances illustrated, and it need not, therefore, be repeated. It is sufficient to direct attention again to the facts that the fat seems to be an especially vulnerable portion of the heart, and that disease is even more prone to arise upon the surface of the heart than in the deeper portions. This peculiarity it has in common with most of the other great organs, as will be shown when the consideration of their morbid lesions is reached.

It would be difficult to exaggerate the importance of fibroid de-

generation of the heart. Some degree of it is a necessary accompaniment of extreme old age; and, on the other hand, no period of life seems too early for it to show itself if the requisite conditions arise. Fibrosis in the heart necessarily interferes with the efficient performance of its function, for the morbid fibroid tissue always replaces muscular tissue if it is not partially formed by an actual conversion of muscle. Some of these peculiarities are graphically demonstrated by the illustrations.

Hollowing and unnatural tenuity of the muscular fibres are forms of degeneration of the heart which are very common. The importance of degeneration of the cardiac walls has not been heretofore underestimated, for no one has bestowed thought upon the subject without appreciating that anything which weakens the heart-muscle strikes a blow at the very root of its power.

Although many writings upon heart disease are pervaded by a tone which shows that the authors were impressed with the great importance of degeneration of the cardiac walls, the subject has not been formulated, and as yet but few well-established facts in connection with it have been collected. The number of hearts microscopically examined by me has been sufficiently great to warrant the assertion that morbid hollowing of the muscular fibres is an exceedingly common lesion. The disease has been recognized for some time, and is generally called vacuolation and attributed to hyaloid degeneration. It is very destructive of the muscle if it attains any great degree of development. This is conclusively proved by the illustrations, which show fibres so completely excavated as to convert them into thin-walled tubes. It is not possible as yet to know its origin, nor to watch all the various steps of this singular disease. Certain facts, however, have been ascertained. The pigment which in elderly persons is always present to some extent in the fibres lying adjacent to the poles of their nuclei, and the fact, to which I have directed attention, that the capillaries penetrate the muscular fibres, must have an important bearing on the process of hollowing, for the part of the fibres that becomes hollow is that ordinarily occupied by the pigment and through which the capillaries pass. It was said in the earlier portion of this chapter that the most probable explanation of the hollowing of the fibres is that it is a cystic degeneration, the hollow portions of the fibres being minute cysts which originated in the capillaries,—that the hollow spaces, therefore, are capillary aneurisms. This is only a theory, for evidence has not been collected sufficient to

prove it a fact, but the more one considers the anatomical relations of the fibres with the blood-vessels the more probable does it seem that such is the correct explanation. The pigment at the poles of the nuclei is so much like altered blood which has exuded from the vessels, as blood is found in other parts of the body in states of disease, that it is impossible to avoid the thought that it may have some relation with the blood. As yet we know nothing of the origin and meaning of the pigment. Perhaps further study of the development of muscular tissue in human and other mammalian embryos will some day lead to a complete explanation. The occurrence of cystic disease of the heart, which has been fully established (page 75), is a curious and interesting phenomenon. Cysts in the heart are probably very rare.

The most important conclusion I have reached is that "compensatory hypertrophy of the heart," as it is ordinarily described and understood, has no existence. All hypertrophied hearts are degenerated and weakened. This position will be very difficult to establish, because of the prejudice that exists in favor of old beliefs to the contrary which have been so long accepted. If it were possible to divest the mind of preconceived opinions and thus approach the subject entirely unbiassed, it would be much less difficult to reach a just conclusion. When auscultation began to be practised and cardiac murmurs were heard, it was soon discovered that their existence almost certainly indicated distortion of the valves. The obviousness of the murmurs, which if loud can be distinguished by a tyro, and the discovery of their connection with changes of the valves, soon gave rise to an exaggerated estimate of the importance of valvular disease. The minds of students of heart disease were occupied with the valves almost to the exclusion of other forms of disease. Every affection of the heart was made to centre in the valves and was explained as having originated from valvular disease. More lately it has been learned that valvular disease may be by no means so dangerous as was formerly supposed, and it is now well established that valvular distortions of such a character as to produce loud murmurs may exist in youth and yet the individuals live in good health to old age. The consideration of such cases ought to have induced a fuller realization of the fallacy of the use, or rather misuse, that has been made of the laws of hydrodynamics. It has been taught and almost universally accepted that regurgitation, which throws extra work upon the walls of the cavity of the heart which is behind the leaking valve, is invariably answered

by nature by an increase of muscle, that the walls of the cavity thicken and grow in strength, that hypertrophy results, and that it is compensatory. It is my belief, founded on observation, that regurgitation does not always cause hypertrophy. If this can be shown to be true, the theories in regard to compensation become untenable. The doctrine that muscles increase when called on to perform severe labor has been pushed much further than is justified by the facts. The truth is, muscles improve in efficiency much more than they increase in bulk and weight. Exercise develops the muscles of a man in good health so that it becomes possible for him to perform feats of strength which would have been impossible without the requisite preparation; but this quality is restricted within narrow limits, and the actual increase of the muscles when exercised is not great, while the individual frequently loses weight. Few men can become superior athletes, and if it is attempted to make one of a person unfitted for it he rapidly becomes "stale" and deteriorates. No development of the muscles of an athlete trained for contest, or of any special set of muscles like those of the arm of a blacksmith or of the upper arm of a file-striker, is comparable to the increase in size and weight of the heart in hypertrophy which is said to be compensatory and conservative! Nor is any allowance made for the fact that hypertrophy of the heart occurs only in the diseased. Upon general principles it seems unlikely that the heart can in disease increase so wonderfully in size and strength to compensate for the harm done by such a defect as a leak, when the most healthy men, even if every opportunity is given them and there is no disease to interfere, can increase the bulk of their muscles so very little, and when, besides this, even among those carefully selected, men often fail under training and the muscles dwindle. It has never been demonstrated that the hypertrophied heart pumps with increased force, or that the pressure within the arteries is raised. Such a demonstration could be made only by the introduction into an artery of an instrument of precision to measure the blood-pressure; and circumstances render this inadmissible. That the arterial blood-pressure is increased when the heart is hypertrophied is inferred because the cardiac impulse becomes heaving and forcible, and because the pulse when felt with the finger imparts a sensation as of fulness and has a bounding character. The question is not asked how much of the heaving motion is due to increase of size of the organ which has become too big for the chest. Nor is it asked if the impression of "high-tension pulse" may be due to thickening and change of character of the

arterial walls. Whatever may be thought of that which has been alleged in support of the opinion that compensatory hypertrophy of the heart does not exist, there is another and a more objective side from which the question may be approached,—the investigation of the actual physical condition of enlarged hearts. Both the gross and the microscopical appearances of hypertrophied hearts show that the muscular tissue is always diseased. It is almost certain that in hypertrophied hearts the number of muscular fibres is increased, and this has for a long time been the opinion of pathologists.* From this fact it has been argued that the heart must be strong, and without further consideration of the many complicating circumstances the compensatory character of cardiac enlargement was assumed. Compensatory hypertrophy is a convenient and attractive theoretical possibility, and it is probable that if a healthy athlete were killed when in the perfection of training, his heart would be found to be slightly larger and heavier than before the training was begun; its condition of pliability and muscular tissue would be perfect; but it is not conceivable that the healthy heart of an athlete could attain the size of the hypertrophied hearts of diseased persons, or could in the most distant way resemble the deformed organ called the *cor bovinum*. In every respect the appearance of the hypertrophied heart contradicts the assumption of increased strength. The walls, though thick, are generally hard and stiff, and the heart has lost its pliability to such an extent that the cavities stand open. It is most improbable that it is able in such a condition to empty itself of blood. The contractions are inefficient squeezes that expel only a small portion of the blood from the cavities, instead of the nearly complete closures that take place in the healthy condition. The muscle is of unnatural color and is easily torn. Thick cardiac walls, enlarged cavities, and very soft muscular substance are the features of another common form of heart disease. Such a heart tears easily, and when removed from the body falls into an almost shapeless mass, so that it is hard to distinguish its natural form. This is not suggestive of unnaturally great strength, although the heart may be of greatly increased size and weight. When a piece of the thick and heavy wall of an hypertrophied heart is subjected to microscopical examination, it is never found healthy. It is unnecessary to repeat in detail what has already been said in regard to the

* Pathological Anatomy, by Samuel Wilks and Walter Moxon, Lindsay & Blakiston, Philadelphia, 1875, p. 113.

various minute changes of the cardiac muscle. At least one of the forms of degeneration is certain to be found in enlarged hearts. Cardiac hypertrophy is not the result of an increase in the amount of healthy muscle as nature's answer to the extra work caused by regurgitation through a leaky valve, but of degeneration of the muscle. There is no evidence that the valvulitis and leaking which so often result from endocarditis precede the disease of the muscular tissue which is their invariable companion, and it is well known that in many cases the walls become diseased and the heart enormously hypertrophied and yet all the valves remain perfectly sound. Of the truth of the statements made in regard to the origin of hypertrophy of the heart there should be no doubt in the mind of any one experienced in its study; and if once it is acknowledged that the enlarged heart is always degenerated and weakened, there is no escape from accepting my view that "compensatory hypertrophy" has no existence.

CHAPTER VI.

THE LUNGS.

Of all the organs the lungs are the most delicate and most liable to disease. This is probably because the air has free access to their inner surface, and they are therefore subjected to rougher usage than the other great organs, which are buried deep in the body and protected from ordinary external irritants. The air is subject to great variation in the degree of its moisture and its temperature, and it often carries in it irritant or poisonous material. The lungs are affected by all these changing conditions of the air in a manner that has no parallel in the other organs. Even the intestinal canal, which has direct communication with the air, is so arranged that but little air ever gets into it. The lungs, like any other part of the organism, are liable to sudden attacks of acute disease, but in the lungs perhaps more frequently than in other organs there will be found some antecedent chronic disease which paved the way and rendered them liable to the acute attack. At very early periods of life, as will be presently shown, processes of degeneration are common which are parallel in every respect with those which occur in persons of more advanced years. Such changes are often of slight extent and may readily be overlooked, but they are none the less important. Emphysema and fibrosis and vascular disease are, so far as is at present known, the common forms of chronic pulmonary decay. A matter of great importance, and one which must never be lost sight of, is the latent manner in which these degenerations progress. Extensive emphysema and fibrosis or vascular disease may often be found in the bodies of persons who had suffered no attack of sickness while these degenerative conditions had been progressing, but had enjoyed sufficiently good health to be able unimpeded to pursue their ordinary vocations. It has already been pointed out that there are recognizable physical differences of appearance between the hearts of the young and those of the old. The same is true of the lung. As life progresses, the amount of fibrous tissue in the lung increases and the actual number of the air-vesicles becomes less, and at the same time the supply of capillaries to the walls of the air-sacs becomes less

abundant and less efficient. All this is true, but it is very difficult to make an ocular demonstration of it. Emphysema and fibrosis as names of diseases are terms which are useful and probably necessary to describe physical conditions which are easily recognized by the unaided eye. In descriptions of them in text-books allusion is usually made to diseased conditions of the blood-vessels as common accompaniments. The likelihood, however, is that these two widely different-looking conditions are the same disease, or only the varying results of a single cause which underlies them. They are not more unlike each other than are scirrhus and some of the forms of soft fungous cancer, and yet no one doubts that both of these are properly classified as one disease. Emphysema has commonly been described as secondary to some other disease, but too much emphasis has been placed upon the presence of obstruction of the bronchial outlets from the air-sacs and consequent enlargement of them by internal mechanical pressure as an absolute necessity to the production of emphysematous dilatation. There is no good reason for supposing that mechanical obstruction is a necessary feature in the production of emphysema; on the contrary, it is likely that it arises as a result of pure fibrosis and degeneration. The possibility of the existence of acute vesicular emphysema without change of structure of the alveolar walls may well be doubted. For all practical purposes, at any rate, such a disease does not exist, for, even supposing that there was a mechanical obstruction to the bronchial outlet of a portion of the lung, with resultant dilatation, the dilatation could hardly have begun before the tissues would suffer from the stretching so that structural change would result.

Fibrosis of the lung is generally classified and described in connection with phthisis pulmonalis or as a form of pneumonia rather than with emphysema or as a degenerative condition. From the standpoint of the clinician fibroid phthisis has such positive individuality that many of the most enthusiastic advocates of the theory that consumption of the lungs cannot exist without the bacillus tuberculosis as its original cause have been forced to admit that the fibroid form of consumption may have an independent existence. Pulmonary fibrosis is also described as a consequence of broncho-pneumonia and of the process called pleurogenous interlobular pneumonia. In addition, however, to these conditions, which are perfectly well recognized clinical entities with definite pathological lesions, there will often be found in the bodies of persons dead of chronic disease, and especially

in those with emphysema, an increase of fibrous tissue in the lungs, which, although not always of great extent, is as easy to recognize as are coarser lesions. Emphysema and fibrosis of the lungs are in their full development as unlike as any two processes could well be, and yet the evidence in favor of their intimate association if not of their common origin is overwhelming. Vascular disease must be looked upon as an essential part of both, for it is always associated with them to a greater or less extent.

The cause is at present obscure. Fibrosis, emphysema, and vascular changes are necessary accompaniments of age if life be sufficiently prolonged, and they may reach extreme forms of development without the individual having had any external manifestation of them. Their progress may be absolutely latent, although the individual usually presents the ordinary appearances of growing older. On the other hand, the influence of attacks of inflammation of the respiratory apparatus in producing emphysema, fibrosis, and vascular disease is beyond question very great, whether the inflammation be in the form of pleurisy, pneumonia, or bronchitis. The lungs are capable at every period of life and in each individual of becoming acutely diseased if subjected to a sufficient degree of irritation. The irritant which is the most prolific cause of such disease is the atmosphere, which is liable at all times to extreme changes, but especially in spring, when the weather is most variable and the temperature subject to the greatest extremes. While it is true that entirely healthy lungs may become acutely inflamed if subjected to sufficient irritation, it is important to remember that lungs which have been rendered imperfect by degeneration or a previous acute attack will succumb to an irritation that would have no effect upon healthy lungs. The two conditions acute inflammation and chronic latent degeneration act and react one upon the other in such a manner that it is often impossible in a given case to ascertain which of the two was the original offender. That chronic latent degeneration may originate spontaneously does not admit of doubt, and it is equally certain that an attack of acute inflammation of the lungs may leave them slightly injured, if it does not always leave them more or less imperfect. Such an imperfection, produced by acute inflammation, may be so slight as never to do any harm; it may lie dormant to furnish the basis of origin for subsequent inflammatory attacks, or it may progress after the recovery from the original acute attack as a latent degeneration, which will go on to a high degree of develop-

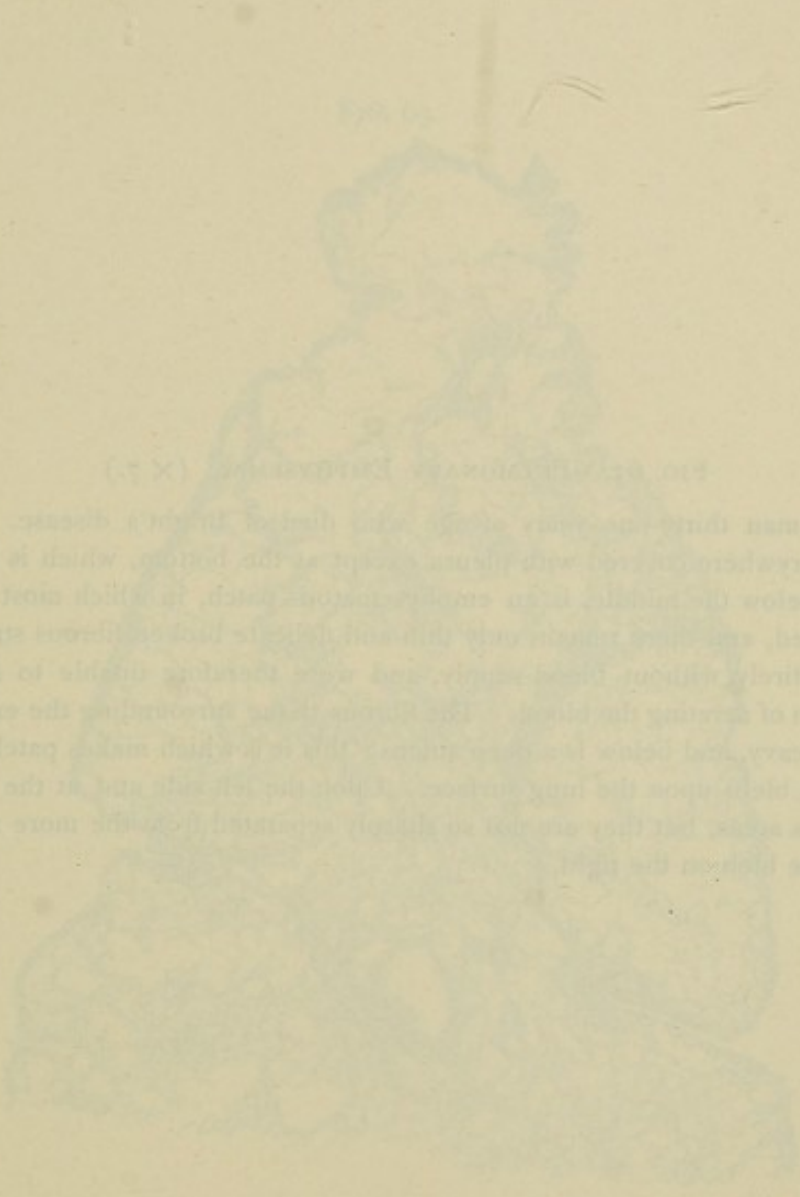


FIG. 63.—PULMONARY EMPHYSEMA. (× 7.)

Lung of a man thirty-one years of age who died of Bright's disease. The portion included is everywhere covered with pleura except at the bottom, which is a cut surface. On the right, below the middle, is an emphysematous patch, in which most of the alveoli have disappeared, and there remain only thin and delicate broken fibrous strands. These strands are entirely without blood-supply, and were therefore unable to subserve their natural function of aerating the blood. The fibrous tissue surrounding the emphysematous patch is very heavy, and below is a deep sulcus: this it is which makes patches of emphysema appear as blebs upon the lung surface. Upon the left side and at the top are other emphysematous areas, but they are not so sharply separated from the more nearly healthy regions as is the bleb on the right.

FIG. 63.

1 mm.

FIG. 64.—PULMONARY EMPHYSEMA. (× 7.)

From a man aged twenty-nine years who died of Bright's disease and peritonitis. The edge below and to the left is a cut surface, the rest is covered by pleura. Above are two emphysematous blebs, one to the right and one to the left of a fibrous band which runs to the top of the section. In the patch to the right the alveoli are exceedingly broken, but few circles remaining, and the fibrous lines are thin and the spaces large, several air-sacs having broken into one. Below are heavy bands of fibrous material, containing blood-vessels and bronchi.

FIG. 65.—PULMONARY EMPHYSEMA IN A YOUNG INFANT. (× 6.)

Lung of an infant six weeks old that died suddenly. The picture is to show the bleb. Its wall is thin and fibrous and without blood-supply upon the free side. Next the lung it is much thicker, and resembles the fibrous wall of a cyst. The bleb was unbroken at the post-mortem examination, and was full of air which seemed imprisoned, there having been no channel for its escape. The curious shape of the line and the breaks in it resulted from imperfect cutting and the way in which the walls were folded in course of preparation. In portions of the lung substance the openings are so large that it seems that they too must be emphysematous. The bottom of the picture shows a cut surface; the other sides are covered by pleura.

FIG. 64.

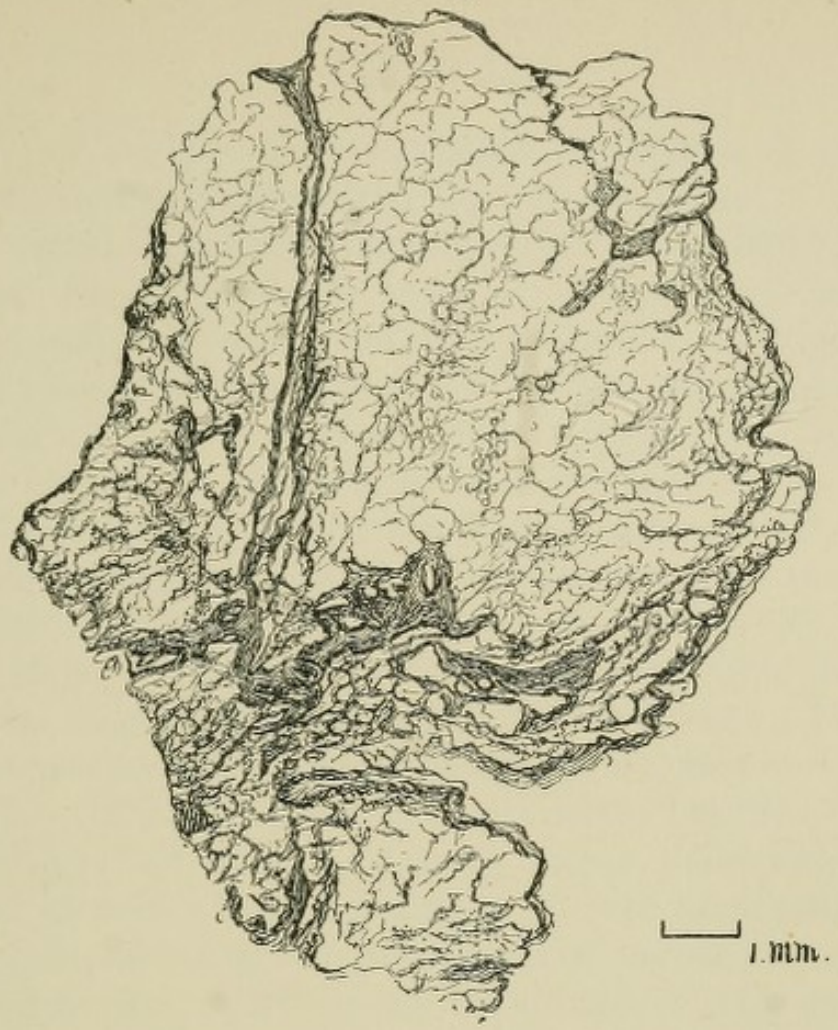
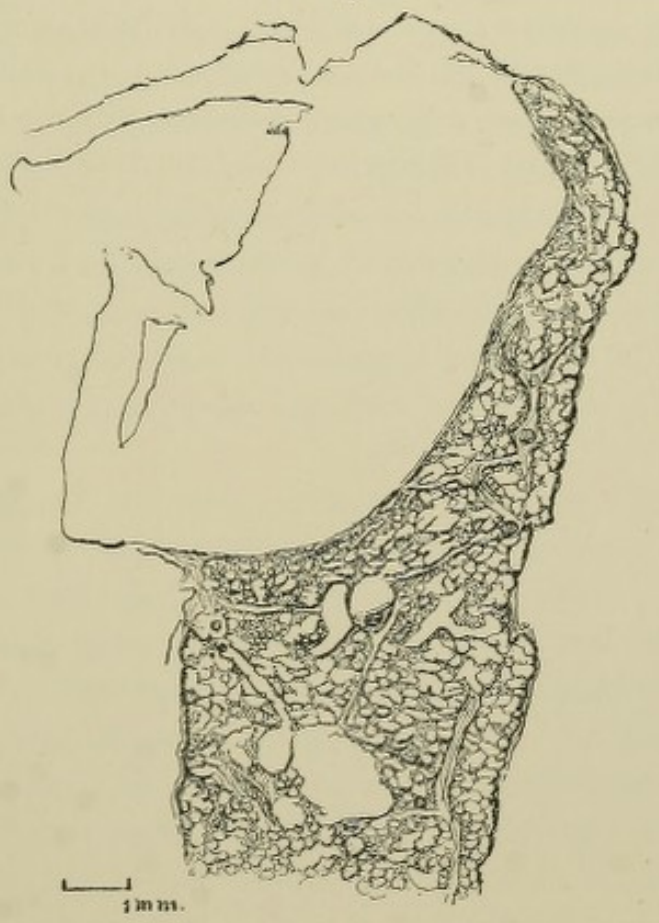


FIG. 65.



ment without any external manifestation in the form of an attack of sickness or even of incapacitating physical weakness.

The illustrations exhibit a number of the peculiarities of disease of the lungs. Fig. 63 represents under low amplification a section of the lung of a man thirty-one years of age who died of Bright's disease. It makes an excellent showing of the ordinary appearances of emphysema when it is fully developed. Upon the right side is an emphysematous bleb which is separated from the surrounding tissue by a thick fibrous layer, and below is a deep sulcus which must have caused the emphysematous bleb to stand out from the surface, as it is common for emphysematous blebs to do when the lung is distended with air. Within the patch of emphysema there are no healthy air-sacs, but only irregular and broken fibrous threads. These threads when examined with higher amplification are seen to be generally without vascular supply, which is so rich in the healthy alveolar walls. The capillaries had atrophied, leaving fibrous tissue which was so ill nourished as to be unable to maintain its own existence; much less was it capable of taking up the oxygen of any air that might be in the dilated air-sacs. Throughout the section is seen an alternation of broken-down air-sacs and increase of fibrous tissue. Such are the common appearances of emphysema, the increase of the fibrous tissue and the destruction of the vascular supply being as much parts of the disease as is the increased size of the air-sacs themselves. Fig. 64 is from the emphysematous lung of a man twenty-nine years old who died of Bright's disease, peritonitis, and other complications. It shows, as the previously mentioned drawing does, that fibrosis is as much a part of emphysema as is dilatation of the air-sacs. There are no healthy air-sacs, the fibrous trabeculæ are much heavier than natural, and the vessels are thickened; but this latter feature of the disease could be satisfactorily studied only by the use of greater amplification.

Fig. 65 presents a strong contrast with the two last described drawings. It is a section of the lung of a previously healthy infant six weeks old that died suddenly of convulsions. The baby was a mulatto that had been nursed by its mother, and no lesion satisfactorily explaining the death was found at the post-mortem examination. There were thrombi in the veins; in the kidneys these were very large, so that the veins were enormously distended, and in the drawing are shown veins in the lung containing clots; but whether thrombosis is to be looked upon as the cause of the fatal attack or

only as one of its effects cannot be known. The drawing presents two special points of interest. In the first place, it shows in a graphic manner the great difference in appearance between the lung in early infancy and at later periods of life. The amplification used was nearly the same for this and the two previously described drawings, and the contrast of appearance is so great that it need not be much dwelt upon. In the infant lung the amount of solid tissue is greater and the amount of air-space less relatively than in the adult lung.

The second point of interest is the existence of emphysema in an infant of six weeks. The lesion certainly can be classed only as emphysema, for with the present understanding of diseases of the lungs no other term describes such an enlarged air-bleb as the one represented. This bleb is bounded upon its free side by a thin fibrous membrane which is entirely without blood-supply, while upon the side next the lung is a thick layer of fibrous tissue which is not richly supplied with blood.

A strange phase of the clinical admixture of acute and chronic disease is illustrated by Fig. 66; this represents the lung of a man twenty-six years old who died of typhoid fever. Most of the air-sacs of natural size which are included in the drawing contain a good deal of cellular and fibrinous exudate, and in other portions of the lungs the alveoli were filled with blood. This condition of things is almost universal in the lungs of persons dead of typhoid fever at any but the earliest periods. But besides the exudation, which was an acute process, the illustration shows a group of air-sacs which are much dilated, and of these the walls are fibrous and heavy and in places broken, so that the number of vesicles has become much less than when the same region was healthy. The broken condition of the alveoli and the thick, fibrous, avascular tissue around their walls are very striking.

Another notable feature is that this emphysematous area is very much pigmented. Although the lung tissue is astonishingly tolerant of the presence of pigment, and often such quantities of it are present in lungs otherwise apparently healthy as to make them almost black, it seems to me that pigment is frequently a source of disease. It is common to find evidence of inflammation or degeneration around pigmented areas, and it is not impossible that the pigment represented in the illustration was the cause of the degeneration that had occurred. The emphysema, fibrosis, and decreased vascularity must have been the results of chronic degeneration, and must have ex-

FIG. 66.—PULMONARY EMPHYSEMA AND FIBROSIS IN A YOUNG MAN DEAD OF ACUTE DISEASE. (× 25.)

Section of lung of a man of twenty-six years who died of typhoid fever. The upper curved edge is covered by pleura which is much thickened and pigmented. There is general cellular infiltration, most of the alveoli being nearly solid. The unusual feature of disease is that there are large emphysematous cavities with thick fibrous walls which are entirely avascular.

FIG. 67.—FIBROID SURFACE OF THE LUNG. (× 21.)

From a man of fifty-seven years who died of Bright's disease. The pleura (*p*) can be distinguished only to the left of the centre. It is evident that the fibrous material grew partly upon and partly underneath the pleura; between *i* and *k* is epipleural and between *k* and *l* subpleural growth. The subpleural fibrous tissue contains many nuclei, and there are blood-vessels in both the epipleural and subpleural layers. The line of separation of the two fibrous layers is very distinct, and at places along it there is much pigmentation. Below *l* is the lung tissue.

FIG. 66.

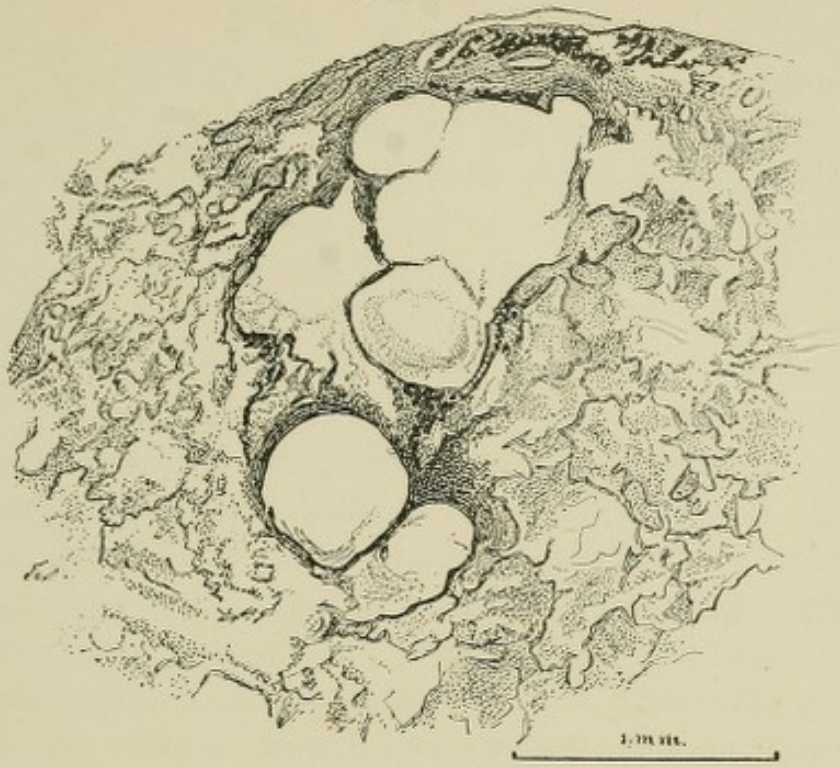
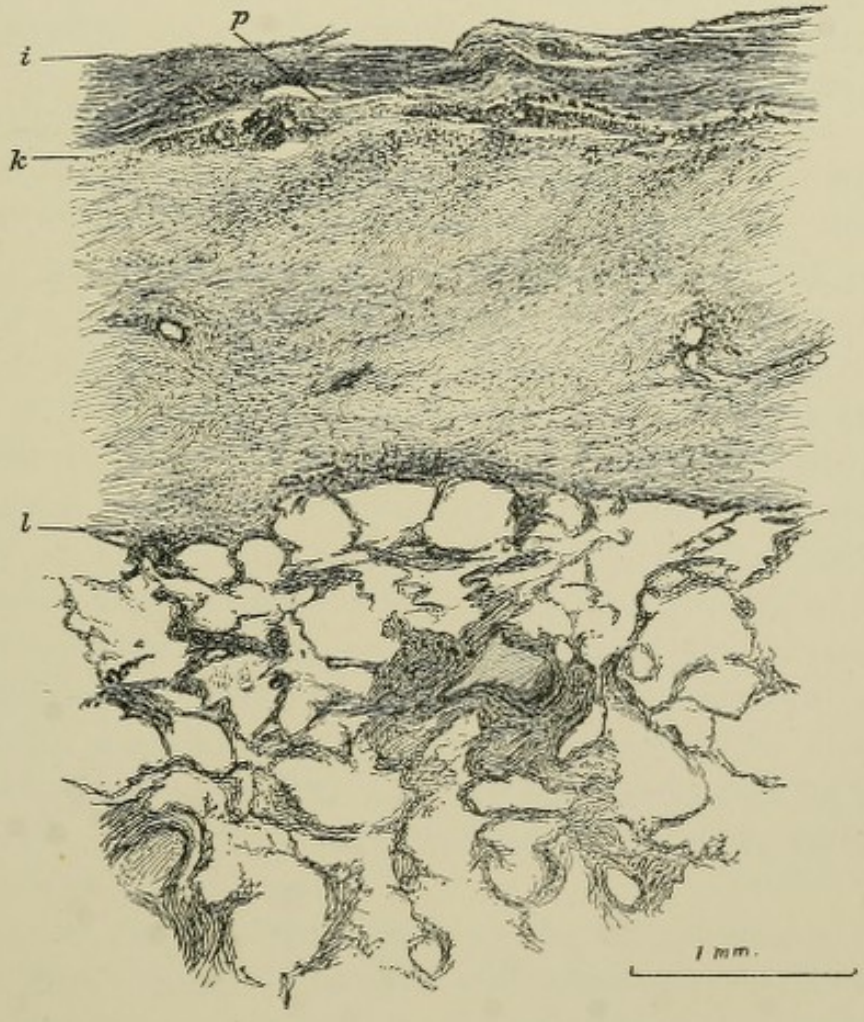


FIG. 67.



isted in the individual for some time before he was attacked by the typhoid fever of which he died. The case, therefore, affords evidence of the correctness of the statement that lesions of chronic disease are commonly found in those who have died of acute attacks and in whom the clinical history reveals no previous illness.

In Fig. 67 is represented an entirely different phase of fibroid disease. It is of the lung of a man fifty-seven years old who died of Bright's disease after a prolonged illness, and in whom there was fibrosis of the most extreme degree in many organs and tissues, with numerous calcareous deposits in many places in the body. The fibrosis shown in the illustration is of the form which is a part of pleurogenous interlobular pneumonia. Upon the surface of the lung and occupying the position of the pleura is a thick layer of fibrous material, which looks at first sight as if it was due simply to pleural thickening. More careful examination reveals, however, that it is of more complex origin. The fibrous layer is seen to be composed of two strata of different appearances, and at one place (see description of figure) the pleura can be distinguished. The situation of this portion of pleura which remains shows that part of the fibrous tissue grew upon and outside of the pleura, while another portion grew below it and therefore at the expense of the lung.

The epipleural fibrous tissue is thick and dense, and in structure similar to that of the fibromas that are so commonly found upon the surface of the lung and spleen, while the subpleural portion is of a structure much less dense. Along the line of contact of the epipleural and subpleural layers, which is the situation of the pleura, there is much pigmentation. When the section is examined with different amplifications along the line of junction of the lung with the subpleural fibrous tissue, it is plainly seen that the fibrous tissue grew at the expense of the lung. Alveoli can be seen with their walls thickened and variously filling up by the growth of fibrous tissue, the porous lung being converted into solid fibrous tissue. The loss of efficiency of the lung from such a degeneration must be very great, for, in addition to the direct reduction of the amount of tissue capable of performing its function, the freedom of its motions must be greatly impeded by such thickenings upon its surface and along the lines of the trabeculæ.

Figs. 68 and 69 represent a species of pulmonary fibrosis which in its most salient features is different from the forms that have been considered. The lung is so much changed as to be almost un-

recognizable. It has lost its naturally porous and open appearance, and is nearly solid. The vessels are thickened, some of them so much that the calibres are almost closed, and the pleura is greatly thickened. Such tissue is not like that which grows from the pleura and fibrous trabeculæ of the lung in pleurogenous interstitial pneumonia, nor has it any resemblance to emphysema, and yet there is nothing in its appearance to forbid the belief that the region had previously been emphysematous. The general character is that the lung had become almost evenly solid. There are, of course, remains of the natural open structure, but such a degree of solidity could have been attained only by a universal growth of the fibrous tissue which composes the alveolar walls, thickening them and in most places encroaching upon the air-spaces to their obliteration. The thought that emphysema might have been the forerunner of such generally diffused solid fibrosis is interesting, and it would be hard to prove that such was not the case. When it is recollected how greatly morbid fibrous tissue (cicatrix) contracts and how irresistible this tendency is, it seems very probable that portions of lung which had been made porous but fibrous by emphysema might sometimes become more fibrous and shrink to solidity, if other disease did not step in to kill before this result was reached. The form of pulmonary fibrosis illustrated is very common in cases of Bright's disease of long standing and in other chronic diseases characterized by the growth of fibrous tissue, and it is much more frequently found in the old than in young persons. Fig. 68 is a section of the lung of a woman sixty years old who died of Bright's disease. The pleura is much thickened, and part of this thickening consists of material like that of ordinary fibromas, such as are common upon the capsules of organs, while at other areas the thickening was at the expense of the lung, the fibrous growth having been from the surface downward into the lung. The pleura is bent so as to form a deep sulcus upon the surface. Fibrous tissue as it grows is apt to produce such irregularities. The vessels are exceedingly thick-walled, and, as has already been said, the general appearance of the tissue is of such solidity that it no longer looks like lung. Fig. 69 is a section of the lung of a negro woman about seventy years old who died of fibrosis of the heart, lungs, liver, spleen, and kidneys after several years of feebleness and illness. The same general characteristics are presented,—diseased vessels, thickened pleura, and general evenly diffused fibrosis; but besides these the lung is pigmented, and there is a

FIG. 68.—FIBROID LUNG. (× 16.)

From a woman of sixty years who died of Bright's disease. *a* and *b* are the pleura, which is greatly thickened, and there is a deep sulcus, the result of shrinking and twisting. At *a* the thickening is of the pleura itself, while at *b* the growth is almost entirely subpleural and has taken place at the expense of the lung. The blood-vessels throughout the lung are thick and partially closed by endarterial growth. Most of the tissue is a dense fibrous material without resemblance to the open loose-meshed appearance of healthy lung. Air-spaces capable of having performed their function do not seem to be present.

FIG. 69.—FIBROID LUNG. (× 16.)

From a negro woman of about seventy years who died having fibrosis of the heart, lungs, liver, spleen, and kidneys. All of the lung included is very fibroid, there being no natural alveoli. *v*, a vessel with thickened walls. Other thick vessels are included, but, as they are of smaller size, they are not easy to distinguish without greater amplification. *p*, the pleura, which is greatly thickened. Below *g* there is a mass of fibrous tissue in the lung which is continuous with the pleura, from which it appears to extend inward.

FIG. 68.

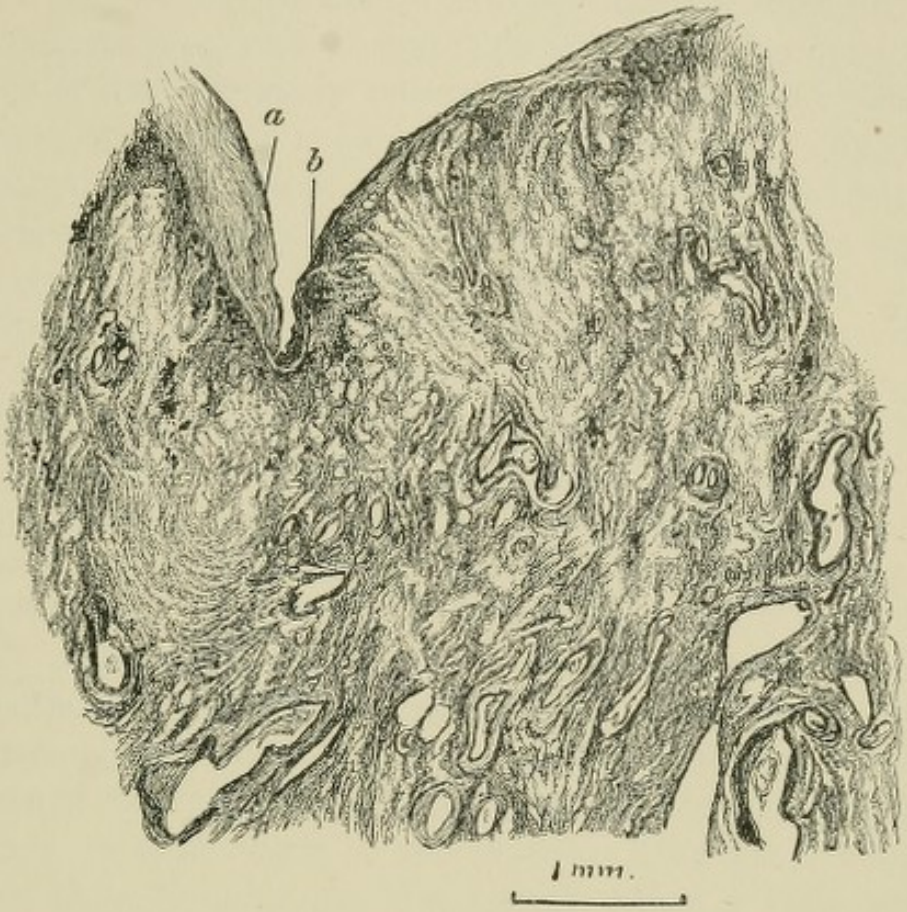
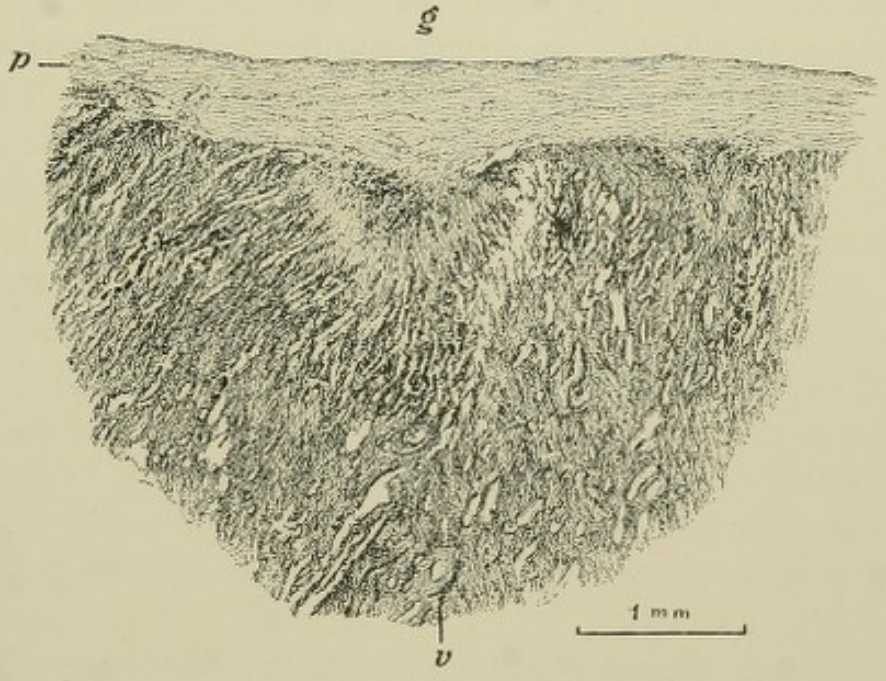


FIG. 69.



growth of fibrous tissue which is continuous with the pleura and extends from it deeply into the lung. A fibrous growth extending from the pleura into the lung such as that depicted is evidently not a thickening of one of the pulmonary trabeculæ, but is a fibroid invasion of the lung tissue itself, which is liable to occur at any part. The growth of fibromas upon the surfaces of organs, the ordinary thickenings of the capsules, and the extension of fibrous growths from the capsules into the organs are very interesting phenomena. Whether disease has its starting-point in such growths, or whether these growths are only secondary effects, is a question impossible to answer, but the answer might point out the road to valuable knowledge. Fig. 70 represents a phase of disease entirely different from any heretofore shown. It is from the wall of a cavity in the lung of a man twenty-six years old who had pulmonary phthisis and died of meningitis. Ordinarily, tubercular lung tissue is fibro-cellular and is more or less rich in cells according to the manner of its growth. In the portion of lung represented the pleura is thickened and somewhat cellular, there is pigmentation, and the cells generally are large, very numerous, and of unusual appearance, many of them having the protoplasm unstained, and in some there is no nucleus. They are of the same character as those forming the new growth within a lung arteriole already described (page 53). Such cells are peculiar to tissue which was of very rapid growth. The amount of fibrous material is less than is usual in tubercular tissue, and there are two peculiar nests of cells, each surrounded by a fibrous envelope. The cells are arranged in a somewhat circular manner, or, to use a botanical term, whorled (the drawing does not make this very clear). The appearance is very like that of the pearly bodies of skin cancer. Circular masses of cells of this character are common in the healthy skin of young infants. A similar growth of cells has already been described (Fig. 38) which was found in the wall of a minute vein. There is a tendency for cells to assume this circular arrangement when there has been rapid growth. The lesson taught is that these circular cell-nests are found as a result of diseased growth in the walls of veins, in skin cancer, in the walls of tubercular lung cavities, and in the healthy skin of young infants. We should, therefore, be careful how we ascribe a specific character to them.

The arteries and veins of the lungs are naturally much thinner-walled than those of other parts, and this is especially true of the nutrient vessels, which are derived principally from the bronchial

arteries, and belong, therefore, to the systemic circuit, as well as of the pulmonary arteries and veins. The thinness of the walls is more noticeable in the pulmonary vessels than in the nutrient branches because of their larger size.

It must have struck every one who has been present at many post-mortem examinations that in the great majority of instances the lungs contain much blood. If the aid of the microscope is invoked and sections are examined, it is the exception to find the lung of any one who has died a natural death without a greater or less amount of blood lying in the air-sacs. Such a condition is always the result of disease, for naturally the blood should be inside the vessels alone. The amount of blood in the pulmonary alveoli after death varies infinitely. There may be a few scattered red corpuscles, or the spaces may be distended with them so as to be impermeable to air. Occasionally lungs are found with alveoli entirely filled with solid masses of blood-corpuscles except the most central portions, which remain empty. The appearance of such specimens is peculiar. In tissue stained with carmine the blood retains the yellowish-brown color which it ordinarily has in dead tissues, and presents the appearance of many closely appressed circles resembling a mass of frog's eggs. Such effusions must have occurred rapidly during the last few hours of life, for otherwise there would be some evidence of separation of the corpuscles so that they might have been reabsorbed or have been discharged as expectoration. The direct cause of death in the great majority of instances is effusion into the lungs. By this is meant that the final and immediate cause of death is the escape of blood and serum into the lungs to such an extent that sufficient air to maintain life can no longer be obtained, and death results from want of air as much as it does in a man who is seized by the throat and his windpipe closed until he is dead. It is only in the case of sudden death which results from the cessation of action of the brain or heart that the lungs are found light and spongy and wholly free from effusion. Sudden death may result from the destruction of the brain or heart by injury, or because disease causes them to cease suddenly to perform their functions. The heart, it is well known, may instantly cease to beat, and death result in a few moments, and the brain, as a result of a tumor or other disease, may suddenly cease performing its function, causing instant death. No other death is so sudden as that which follows destruction of the medulla oblongata. With the exception of those due to the brain or the heart, it may be said that all other deaths

FIG. 70.—GROWTHS IN THE WALL OF A LUNG-CAVITY. (× 250.)

From a man of twenty-six years who had phthisis and died of meningitis. *o* are the growths, which consist of nests of cells not unlike those of the growths in the wall of a vein depicted in Fig. 38. *d*, *d* is the lower boundary of the pleura, which is much thickened and more cellular than natural. *j* is a vessel containing blood-corpuscles. *t* indicates masses of pigment. The cells of which the tissue is composed are large, and many of them consist of a nucleus surrounded by a space which appears to be empty, and outside of this is the cell-envelope. The appearance of other cells is that of an envelope with nothing inside it.

FIG. 70.

result from the lungs. This statement for all practical purposes and from the stand-point of the clinician is true, although physiologists will describe death as a much more complicated process.

In the ordinary acute and chronic diseases it is wonderful how much the organs can bear. Various inflammations may exist, the abdominal cavity may be filled to distention with liquid, the pericardium may contain serum, the heart may beat with extraordinary rapidity or the greatest irregularity, the lungs themselves may be surrounded by liquid in the pleura, and life still be preserved, but if the pulmonary vessels cease to perform their functions and allow the transudation of much blood the result is speedy death.

It has sometimes been thought that the blood found in the air-cells resulted from post-mortem transudation, but for one who has often watched death and seen that the only sure sign of its near approach is the filling of the lungs, and that this always occurs unless the death is sudden from the heart or the brain, such a belief is unreasonable. The condition which is described as being *in articulo mortis* in the vast majority of instances comes on only when the contents of the pulmonary vessels begin to escape into the lungs.

The observation is a curious one, and worthy of being recorded, that in the lung effusion of blood is especially liable to occur directly beneath the pleura, just as it is apt to occur under the capsules of other organs, as, for instance, the heart, liver, spleen, and kidneys. This is adverted to in the description of other organs, but no explanation of it can be found. In a case in which death resulted from acute cholera morbus I found extensive ecchymoses beneath the capsules of the heart, lungs, liver, and kidneys. Microscopical examination showed that these ecchymoses had no depth, that they did not penetrate into the substance of the various organs, but lay almost entirely between the capsules and the subjacent tissues. In many acute and chronic diseases hemorrhage beneath the capsules of the organs is frequently found. Associated with hemorrhages beneath capsules, and evidently a part of the same process, it is common to find areas of inflammation or of pigmentation and thickening of the capsules. Capsular thickenings are frequently the seats of origin of disease, as has already been said, inflammation or fibrosis beginning upon the surface and extending deeply into the substance of the lung. The question of the relation of pulmonary fibrosis to consumption of the lungs is one of the highest importance; it is discussed elsewhere (page 89). Lung fibrosis sometimes coexists with amyloid degenera-

tion of the other organs, and it is hard to escape from the belief that they are allied diseases or proceed from a common cause.

The lung, like all the other organs, is liable to attacks of inflammation, and, as has already been pointed out, it is even more vulnerable than any of the other organs, for the reason that it is exposed to the direct influence of the atmosphere with which it is constantly filled. The fact has also been mentioned that inflammatory attacks of the lung even when very slight in character may pave the way for more severe ones subsequently, though, on the other hand, they may heal so completely as to leave the lung for all practical purposes uninjured. From what is known of the general behavior of the process of inflammation it is certain that the exudative material deposited in the air-spaces of the lungs as a consequence of inflammation is sometimes imperfectly removed in the process of healing, and is an element tending to produce recurrent inflammation or degeneration.

Pneumonia is a term which is essential to describe a clinical condition with definite pathological changes the result of inflammation of the lungs, and which in its typical form of development is as well defined as any disease. The difficulties, however, of the physician and pathologist begin when the attempt is made to decide to what extent the greatly varied forms of inflammation of the lung are to be included by the term pneumonia. It is not usual at present to classify all inflammations of the lungs as pneumonia, and on this account, and because pneumonia, bronchitis, sometimes phthisis, and many of the chronic degenerations of the lungs are commingled, the employment of the terms at present in use to describe diseases of the lungs is often exceedingly unsatisfactory. A full discussion of this subject belongs, however, more properly to the head of diagnosis.

Emphysema is so intimately connected with fibrosis that the two must often if not always be classified together. It occurs at all periods of life, even in early infancy and in childhood, as, for instance, at twelve years, when the alveoli may be found enlarged and the remaining fibrous material thickened and there may be subacute inflammation of the degenerated part, as shown by the presence of blood and exudate cells. A most important part of emphysema is the decreased vascularity of the dilated air-sacs. Emphysema seems in some instances to serve a conservative purpose in chronic conditions of disease. For instance, in an old case of gouty Bright's disease, in which there were obliteration of the pleural sacs by adhesion, great fibrosis, and emphysematous enlargement of the air-sacs, life was unusually prolonged,

and it seemed as though this was due to the fact that the lungs did not fill up and cause death in the usual way. The lung could not collapse, as it was held open by the pleural adhesions, and its substance was spongy and leathery and avascular to such an extent that it seemed not to have had sufficient vitality to fill up and cut off the supply of oxygen. This has been mentioned also in connection with Fig. 66, which shows large emphysematous sacs remaining empty while surrounded by tissue partly solidified from inflammation. The blood-vessels are very commonly thickened. By practice lesser degrees of emphysema and fibrosis may be recognized by any one accustomed to search for them, both with the unaided eye and in sections for microscopical examination.

Pigmentation of the lungs exists to a greater or less extent in all persons subjected to the conditions of modern civilization, the particles suspended in the atmosphere being inhaled and lodging in the lungs: besides, it is possible that pigment is carried to the lungs and deposited in them by the circulation. It is so very common to find a mass of pigment lying in and appearing to be the centre of irritation in a tubercular area or in a spot of subpleural inflammation, that it seems to me that pigment in the lungs is by no means so harmless as it is commonly thought to be. Like any other foreign body in the tissues, pigment must either become encapsulated and lie quiescent or must form the centre of an inflammation. It is highly probable, therefore, that a deposit of pigment is much more frequently the source of disease than is generally supposed.

A common post-mortem condition is the presence of calcareous deposits in the lung; these may be either near the surface or deeply seated in the organ, and generally the tissue is somewhat puckered and contracted around the chalky material. Such deposits are more frequently found in elderly persons and in those who have been long the subjects of chronic disease. It has been commonly taught that the deposit of chalk in the lung and the surrounding puckering of tissue are to be looked upon as signs that the person had previously suffered with phthisis, and that there had been a cavity in the lung which in healing had puckered the tissue and caused the deposit of the chalk. Such a conclusion has seemed to me not to be warranted by the facts. Although the deposit of chalk in tubercular portions of lung is common enough, on the other hand, calcareous material is so very frequently found in other organs and tissues of the body in places and under circumstances that make it certain that it had

nothing to do with tubercular disease, and the appearance of the chalky deposits in the lungs is so little suggestive of tuberculosis, either present or past, as to make it seem more likely that chalk in the lungs is only the result of disordered action of the organism which allowed the blood to cause it, just as such disordered action may cause the deposits in other places, and that generally it is in no wise related to tuberculosis.

It seems almost superfluous to say that of all the pathological changes that the lungs undergo those produced by consumption are the most important. It is, in temperate climates, the cause of the death of a greater number of people than any other disease. This is not the place to discuss in full the questions of consumption of the lungs, pulmonary phthisis, and tuberculosis. Here all that is necessary is to state briefly something of the character of the lesions. The appearances of the grosser lesions of destruction and of the smaller tubercles or of miliary tubercles are unmistakable, and so are those of sections of tissue from typically consumptive lungs when examined with the microscope. On the other hand, if the question is looked at from a different stand-point, there is nothing whatever in such tissue which is peculiar to it, unless it be the presence of giant cells or tubercle bacilli. The point it is desired to emphasize is that tubercular tissue is nothing but a growth of fibrous and cellular material in which one or other of the two constituent parts preponderates according as the growth has been rapid or slow. Much fibrous tissue and few cells are found if the growth has been slow, and, on the other hand, there are many cells and little fibrous tissue if the growth has been rapid, exactly as is the case in cancers, in which the scirrhous and encephaloid forms constitute the two extremes. Giant cells and tubercle bacilli are the only specific things which are peculiar to tubercular tissue. So far as concerns bacilli, they often cannot be found in a given piece of tissue which is known to be tubercular. Giant cells are not understood. Even now no one knows what they are, although there is every reason to suppose from their appearances and behavior that they are a result of distorted tissue-growth and are not of extraneous origin. It is certain that practically it often happens that in tissue undoubtedly tubercular neither giant cells nor bacilli can be found. Sometimes the most careful examination will fail to show whether a particular specimen was tubercular or not; but the point of greatest importance is that structurally tubercle is only a fibro-cellular growth, and that it is not subject to any greater variation of appearance

than other diseased tissues. Young tubercle is different from old, and that of rapid growth is unlike that which was slow in growing. The greatest difference perhaps is between that which has begun to disintegrate and that which is still active, but in saying this all has been said, and the fact remains that consumption of the lungs and all forms of tuberculosis are morphologically only the growth of fibro-cellular tissue and its destruction.

CHAPTER VII.

THE LIVER.

As the liver is the largest secreting organ of the body, there is every reason to suppose its function is of the highest importance; the consequences, therefore, of any derangement of it are likely to be serious. At the same time it stands to reason that an organ which is so large and so vascular must be exceedingly liable to disease. The condition of the liver in early infancy is quite different from its condition in later life. During infancy it is softer and of a different color. When examined with the microscope it appears to be composed of an even mass of cells, rich in nuclei and giving the impression of an activity of growth which does not exist in older tissue, and there is but little fibrous tissue. Notwithstanding the great difference between the young and the old organ, hepatic disease of chronic form, such as is most common in middle life or in old age, may occur in the young. Disease of this character I have found as early as the fifth month of life, and at nine, ten, twelve, and fourteen years. Chronic inflammation and cirrhosis or fibrosis are types of the class, being common in middle life and in old age. When they occur in children or infants they are generally accompanied by an appearance of premature age.

The commonest morbid change of the liver found after death is that named nutmeg liver. This condition is very frequent in cases of long-standing heart disease; it is generally attributed to obstruction of the circulation, and is called mechanical hyperæmia of the liver. Rindfleisch mentions with approval and makes use of the name given it by Virchow, of red atrophy. Although it is true that the disease is exceedingly common in cases of heart disease in which there has long been obstruction of the circulation, it seems to be going further than is warranted by the facts to assume that it never exists under any other circumstances and that it is always due to passive congestion. The disease is represented in typical form by Figs. 71, 72, and 73. The first includes part of a portal vein with a small branch of the hepatic artery and a minute bile-duct. Around these are grouped several acini, which show different conditions of degeneration charac-

FIG. 71.—DEGENERATION OF THE LIVER COMMONLY CALLED NUTMEG LIVER. (× 50.)

From a negro man of thirty years who died of organic heart disease. The large space in the centre of the picture is the opening of a portal vein. The acinus *r* at its centre has no secreting cells left. *w* indicates the area depicted more highly magnified by Fig. 73. *s* is an acinus like *r*, but that the liver framework, from which the secreting cells have disappeared at the central portion, is filled with blood-corpuscles. A condition parallel to this, but from another section, is shown by Fig. 72. *q* is an acinus in which the tissue is much broken and full of holes; these are cysts, for they are larger than fat-cells and are unlike them.

FIG. 71.

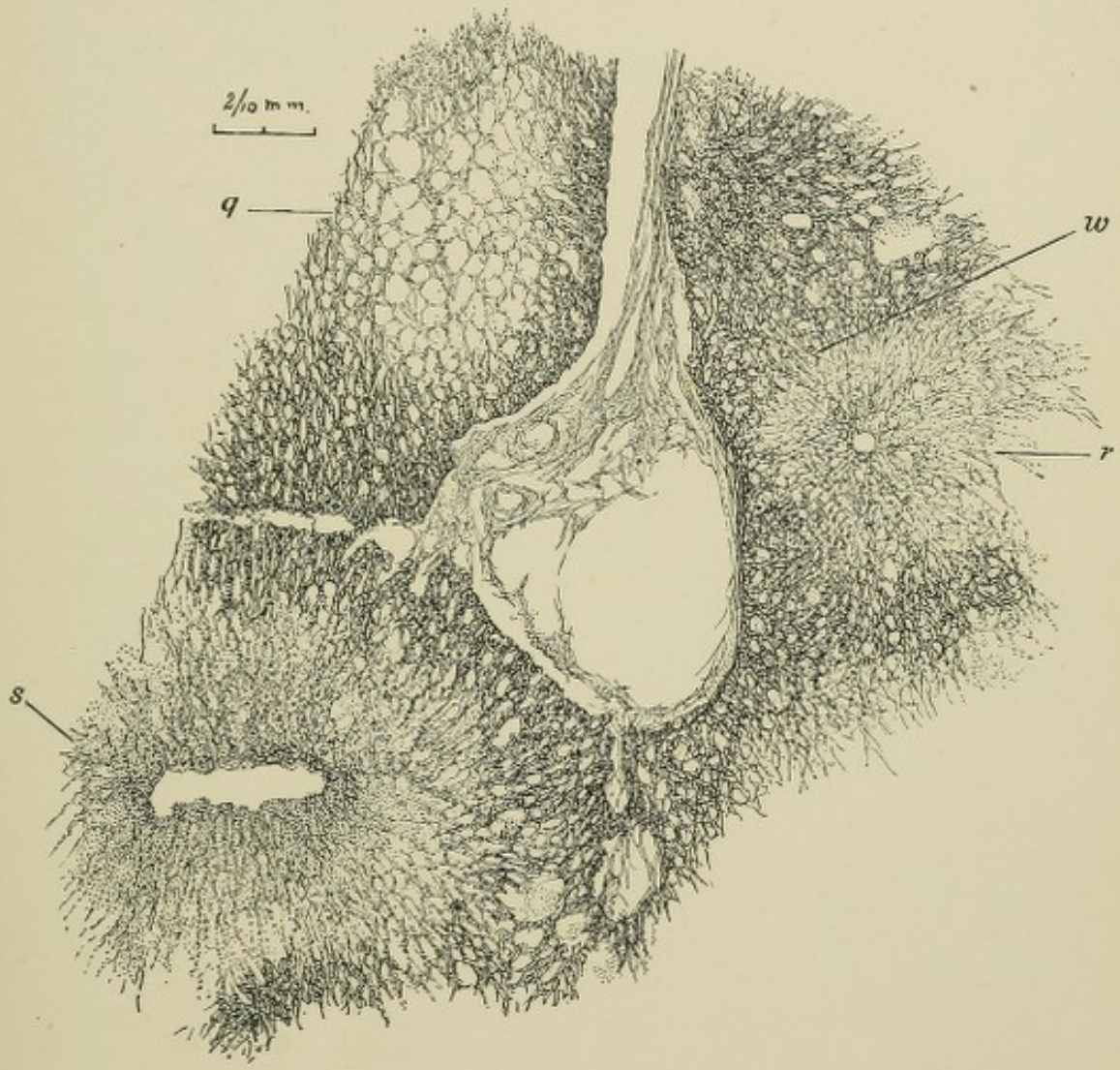


FIG. 72.—NUTMEG LIVER. (× 280.)

From a negro man of thirty years who died of organic disease of the heart. *a* is a portion of tissue from near the centre of an acinus. Everything is overwhelmed with blood, the trabeculæ which formerly contained liver cells as well as the natural blood-channels being filled to their utmost capacity with corpuscles. Nothing remains of the liver tissue but the few scattered cells, which are in appearance precisely similar to those commonly seen in urine and occasionally in cysts. A striking feature is that the portion of the liver which is the most indestructible and the only portion which has persisted is what may fittingly be called the skeleton,—namely, the fibrous material forming the walls of the trabeculæ. This is composed of tubes into which were packed the secreting cells. It appears in the picture as strong fibrous lines, of which two run parallel to each other, forming the two sides of the trabecula. *b* is a region in which the liver substance is disintegrating; it consists of granular matter and secreting cells in various stages of destruction. Perpendicularly from top to bottom the picture is divided; to the left is the region overwhelmed by blood, the central portion of the acinus, while to the right the liver tissue persists, the peripheral portion of the acinus. *c* is a trabecula in which the process of destruction and atrophy of the liver cells can be seen. The fibrous walls of the trabecula are distinct; in the centre is the cord of liver cells, only a single row remaining, and these are so small and so much rounded by pressure that if they were isolated they would not be recognizable as liver cells. Between the fibrous walls and the secreting cells there is a space which contains débris and blood-corpuscles, the blood having escaped from its natural channels and forced its way into the trabecula to destroy the secreting cells.

FIG. 73.—NUTMEG LIVER. (× 280.)

The region *w* from Fig. 71, more highly magnified. A beautiful demonstration of the common appearances of nutmeg liver when the process has reached a more advanced stage than that represented by Fig. 72. Blood-corpuscles are no longer to be seen in the diseased portion, where only the skeleton of liver remains. Were a line drawn from *a* to *b*, it would divide the picture so that the tissue from the periphery of the acinus would lie below and that from the centre above the line. The latter consists of the liver framework containing still some partially destroyed cells. Close examination enables one to follow the remains of trabeculæ upward from the sound into the diseased portions.

Fig. 72

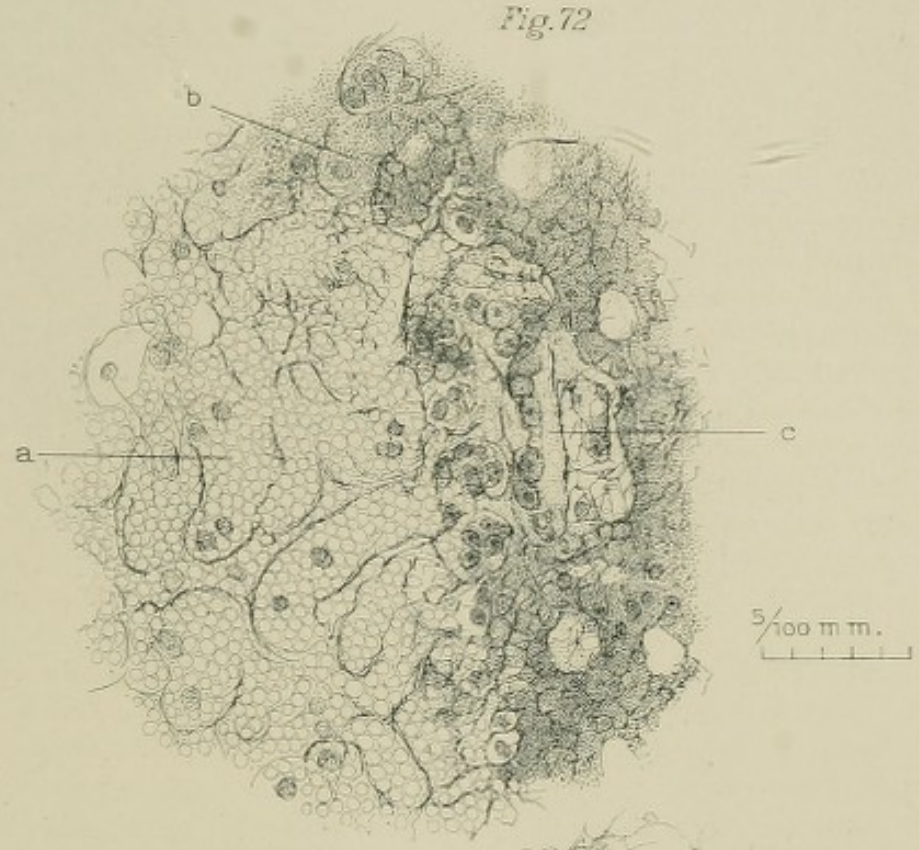
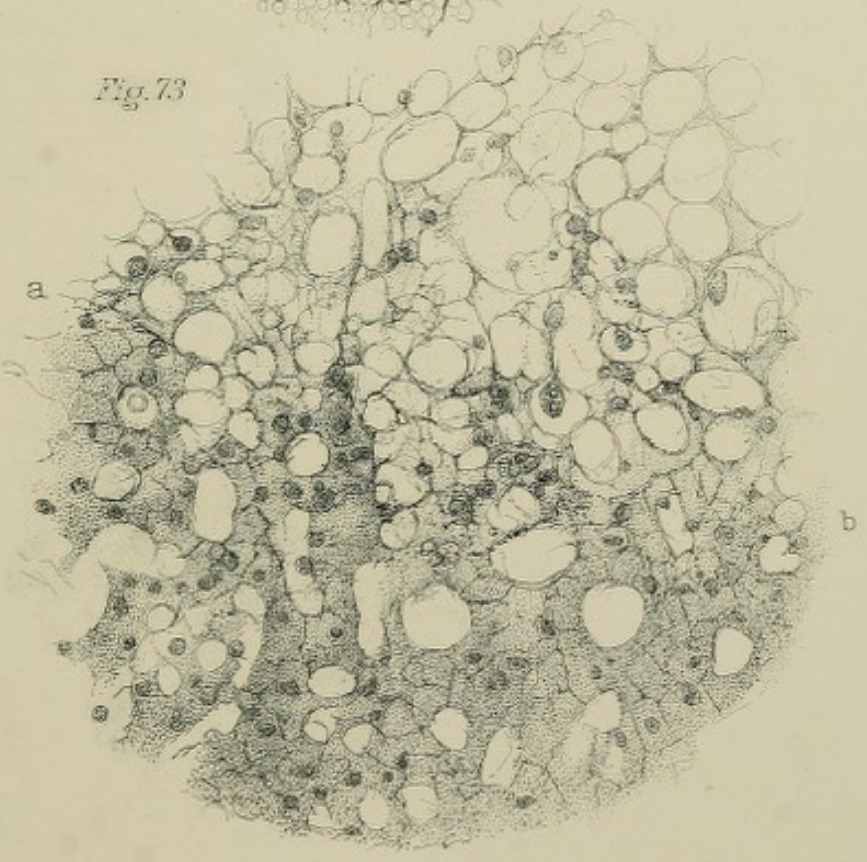


Fig. 73



teristic of the disease. The tissue is unlike healthy liver in one respect: instead of being well knit, there are numerous holes, which produce an open appearance. In one of the acini (see description of Fig. 71) the holes are so large and the mesh-work so open that cystic degeneration is strongly suggested. Such appearances could not be due to fatty degeneration. The existence of these holes is not usually mentioned in the descriptions of nutmeg liver, and yet they are invariably present and its most characteristic feature. Before it is reasonable to accept the congestion theory as a complete explanation of nutmeg liver it is necessary to find a reason for the existence of the holes, and such a reason is not supplied by the assertion either that they are dilated blood-spaces or that they are the result of fatty degeneration. This matter is further discussed in connection with the subject of cystic disease of the liver (page 106). Two of the acini included in the low-power drawing (Fig. 71) demonstrate the ordinary microscopical appearances of nutmeg liver. In one the secreting cells have entirely disappeared from the centre of the acinus, leaving only the framework of the hepatic tissue behind. In the other also the liver cells have disappeared at the centre, but their place has been taken by a solid mass of blood-corpuscles.

The two drawings made with greater amplification (Figs. 72 and 73) show the character and details of such degeneration better than the low-power drawing, in which the enlargement was not sufficient to show individual blood-corpuscles. The upper picture represents liver which appears as if overwhelmed by blood. To the left there are to be seen only the framework of the liver and a mass of blood-corpuscles containing a few scattered cells. To the right the liver cells still remain. In the midst of these cells is a column or trabecula of the secreting cells (see description of Fig. 72, *c*), which demonstrates the process by which they become extinguished. Blood-corpuscles have insinuated themselves between the liver cells and the fibrous framework, which in healthy liver is entirely filled by the cells. The trabeculæ generally consist of a double row of secreting cells, instead of a single one as this does. The ordinary shape of liver cells is well known, and most of those in the picture have it, but those of the column mentioned are rounded and so distorted that they could not be recognized as liver cells were they isolated. The process appears to be one in which the blood-corpuscles escape from the interior of the vessels and are forced into the tissue. They must crush the delicate secreting cells, causing their disappearance and leaving the fibrous

framework or skeleton of the trabeculæ filled with blood. There are also included in the picture a few of the holes in the tissue which have already been mentioned as constituting one of the most striking features in the low-power drawing of nutmeg liver. The lower picture (Fig. 73) is an enlarged view of a portion of one of the acini included in the low-power drawing (Fig. 71). Half of it represents liver tissue which is normal, except that there are more large open spaces than is natural, while the other half is made of liver framework from which almost all the secreting cells have disappeared. The persistence of the framework or skeleton of the liver after the secreting cells have disappeared is remarkable, but perhaps it is only what should be expected, considering that it is composed of a hard fibrous material less easily destroyed than the softer secreting cells. The assumption that all this destruction is the result of congestion and is caused by an overflowing of the tissue by the blood seems untenable. The extent to which such liver tissue can be regenerated is an important question, which cannot be satisfactorily answered at present. The appearances which have been described are the well-known ones of nutmeg liver, or, if the name be preferred, of red atrophy, and the open spaces or holes which have been mentioned are always to a greater or less extent found as an accompaniment of the disease.

Figs. 74 and 75 show the same holes, but under conditions and of an appearance different from those already described. The two portions of liver depicted lay close together, and both contain many of the open spaces. In one the tissue is filled with blood-corpuscles, while in the other none are visible. The hemorrhage was very great, and this is well shown by the drawing. The blood-spaces are all distended, and even the secreting cells were invaded. Blood-corpuscles seem to cover everything, and it looks as if they had forced themselves even into the substance of the secreting cells. There is, however, one striking exception to this: most of the holes remain empty, the blood having been unable to break through their envelopes to fill them. Many, however, are visible which are full of blood-corpuscles like the rest of the tissue. That the holes here shown and those in the liver which had undergone nutmeg degeneration are of the same nature does not admit of doubt, and yet the patients and their diseases and modes of death could hardly have been more different than they were. The patients from whom Figs. 72 and 73 were taken were both negro men thirty years of age who died of heart disease with typical nutmeg livers, while Figs. 74 and 75 are of the liver of a prematurely

FIG. 74.—CYSTIC DISEASE OF THE LIVER. (× 280.)

From a woman of sixty years who died of Bright's disease and had cirrhosis of the liver. Fig. 84 is from the same case. The large spaces are the cysts; some of them contain amorphous material and an ill-defined nucleus, but these are the smaller ones, those of larger size generally appearing to be empty.

FIG. 75.—CYSTIC DISEASE OF THE LIVER. (× 280.)

From the same section as Fig. 74; an adjacent region. Blood has overwhelmed the tissue; the capillary spaces are distended with red blood-corpuscles; the liver cells are filled or overlaid or underlaid by the corpuscles; they even fill most of the cystic spaces, only a few remaining empty.

FIG. 76.—CYSTIC DISEASE OF THE LIVER. (× 55.)

A collection of irregularly divided cysts surrounded by liver tissue; from a man fifty-one years of age who died of perihepatic abscess. At *h* the columns of secreting cells have been compressed by the growing cysts so that they are much narrowed. *g*, a region presenting the ordinary appearances of fatty degeneration, the oil-cells being of large size. *a* corresponds with *x*, *b* with *y*, and *c* with *z*, in Fig. 77, which is a representation of the same region more highly magnified.

FIG. 77.—CYSTIC DISEASE OF THE LIVER. (× 280.)

A more highly magnified view of a portion of Fig. 76; *a*, *b*, and *c* in the latter are indicated by *x*, *y*, and *z* respectively. *x* and *y* are two cysts with a broken wall of separation. At *e* the cyst-wall is composed of partly degenerated liver cells, and much of the wall is of this nature, although at places there is some fibrous material. *z* is the central one of three cavities which are too large to be ordinary fat-cells. *n*, a nucleus in the wall of one of the cavities; the appearance is that generally given as typical of fatty degeneration of a liver secreting cell. *f* presents the appearances typical of fatty degeneration of a liver cell, and surrounding it are others in various stages of the same process of destruction. It seems as if *f*, *z*, and *y* must represent progressively increasing stages of the same process of cystic destruction of liver.

Fig. 75

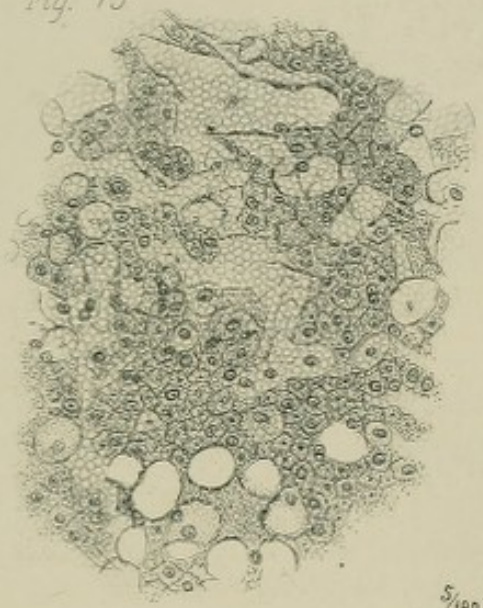
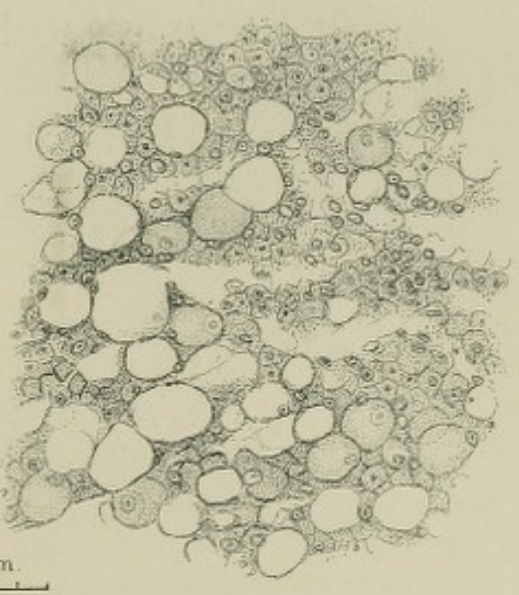


Fig. 74



5/100 mm.

Fig. 76

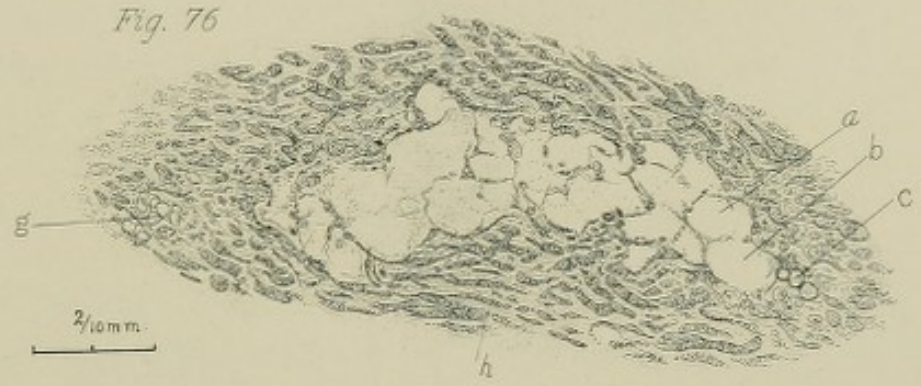


Fig. 77

aged woman of sixty who died of Bright's disease with fibrosis of the heart, lungs, and spleen, and whose liver was typical of cirrhosis of the contracting form. It might be thought that the holes in both cases resulted from fatty degeneration, which is well known to be a usual accompaniment of both forms of disease. Their appearance, however, and their large size forbid such an assumption.

Existing classifications of disease are inadequate to satisfy a mind that seeks precision. Diseases that are commonly considered to be as far apart as nutmeg liver, fatty changes, cystic disease, hypertrophic cirrhosis, and cirrhosis of the contracting form present so many common features that it is impossible not to believe that they are all related, or that there may be a common cause or causes which produce them all. This relationship can be best explained by illustrating the anatomy of the fatty, cystic, and cirrhotic changes before the subject of the general connection of the various diseases is discussed. It must be kept in mind that the holes in the liver heretofore demonstrated cannot be satisfactorily accounted for either as being blood-channels or as due to fatty degeneration, nor can their presence in nutmeg livers be explained by the hypothesis that the disease is the result of passive congestion.

Figs. 76 and 77 are pictures of the liver of a man of fifty-one years who died of perihepatic abscess. The first is a low-power view, and the second represents a small portion of the same field more highly magnified. (See description.) The low-power drawing shows a number of large irregularly divided cavities surrounded by liver tissue in which the columns of cells have been flattened, and in which to the right and left of the large cavities there are areas showing typical fatty degeneration of the secreting cells. The large cavities are cysts. Fig. 77, having been drawn with greater amplification, shows more of the details of structure. The cysts, two of which are included, are connected, as the separating wall is broken. Their surrounding walls are composed of irregular and flattened liver cells and shreds of fibrous tissue. Their size and appearance make it certain that they were cysts and had contained a watery fluid, not oil. There are also included a number of cells showing typical fatty degeneration. Small oil-globules having developed within the cell envelope, the appearance presented is of an oil-globule surrounded by a ring which is composed of the liver cell, and in this the nucleus often is distinctly visible. There are a few of these oil-globules (see description of plate) which are of much larger size than the ordinary ones of fatty degeneration,

and yet much smaller than the cysts shown in the drawing. Careful consideration of the appearances of the pictures and of the tissue from which they were made forces upon the mind the question whether all these cavities may not be only different gradations of the same disease, and whether from the smallest globule of fat, which as seen with the microscope looks like an empty space, to the largest cavity in the tissue, they are not only the progressive stages of one process which has ended in cystic degeneration.

Cystic degeneration of the liver is generally considered rare and something of a pathological curiosity. Cysts of large size are not of frequent occurrence in the liver, but in my experience small ones are not unusual. By this are meant cysts of such size as those which have been shown, or even smaller, being so small that they might elude detection by the naked eye, although if by accident included in a section they would be very striking when seen with the microscope. The theory has been put forward and very generally accepted that cysts in the liver have their origin in obstruction and consequent dilatation of the bile-ducts. It is not possible to prove this theory incorrect, but some time ago I published an account of a case * of cystic degeneration of the heart, spleen, liver, and kidneys in which it was shown that there is ground to suppose that such cysts originate in the capillaries. True cysts, according to the classifications, are those which had their origin in the dilatation of a previously existing duct or cavity, while false cysts are those developed directly in the meshes of a tissue, such as abscesses or blood-extravasations. That the cysts in four different organs in the case mentioned were true and not false cysts was shown by their appearances. It is in the highest degree probable that they were all of the same nature,—that their mode of origin in one organ was their mode of origin in all. In the heart and spleen there exist no ducts or cavities in which cysts could arise except the blood-vessels or lymphatics. Cystic enlargements of blood-vessels are common enough, while almost nothing is known of the origin of such disease in lymphatics. The probability, therefore, that the cysts in the heart and spleen had their origin in the blood-vessels is very great. If they arose in the blood-vessels in the heart and spleen, it is most likely they had the same origin in the liver and kidneys. This train of reasoning, though it proves nothing, leads up to the assertion that in the case of cystic disease under consideration

* Journal of Anatomy and Physiology, vol. xxvi. p. 454.

FIG. 78.—CYSTIC LIVER. (× 5.)

From a man of seventy-seven years who had also cystic disease of the heart, spleen, and kidneys. The cysts are of various sizes and generally appear empty, but some contain amorphous material (*c*). Some of the cysts have well-defined fibrous walls, in others the boundaries are liver cells. This is better shown by Fig. 79, which is the area *b* more highly magnified.

FIG. 79.—CYSTIC LIVER. (× 45.)

The area *b* in Fig. 78, more highly magnified. *d*, amorphous cyst-contents; *e*, fibrous cyst-walls; *f*, liver cells separating one cyst from another. There is great increase of fibrous tissue; *g* is an island of liver cells surrounded by fibrous tissue. The columns of secreting cells have been flattened and narrowed by the fibro-cystic growth.

FIG. 78.

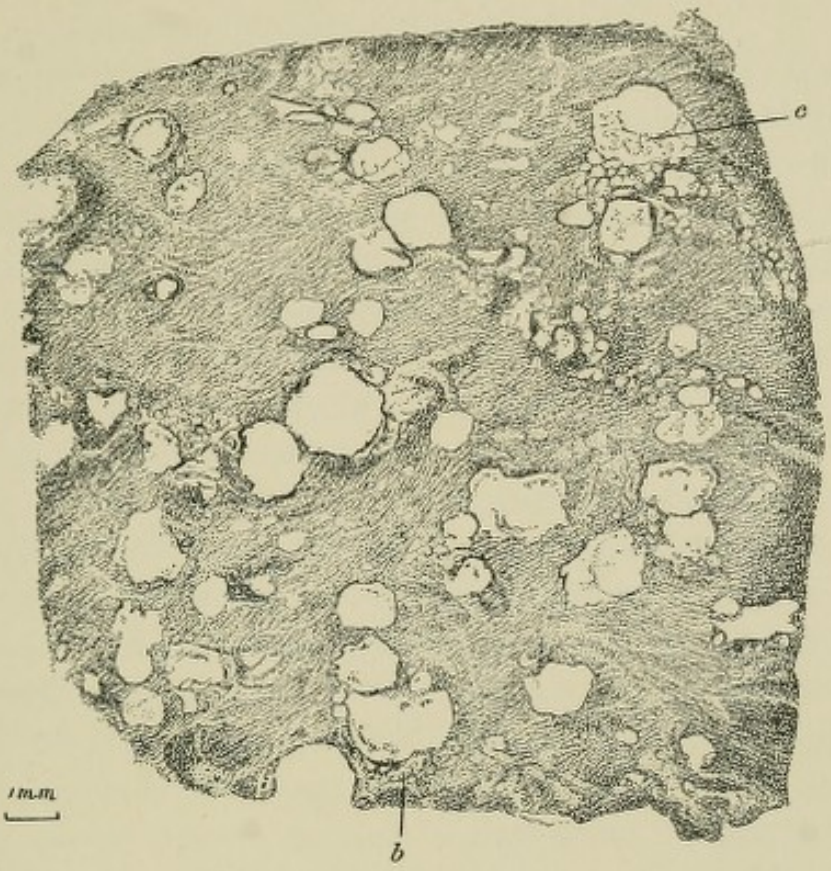
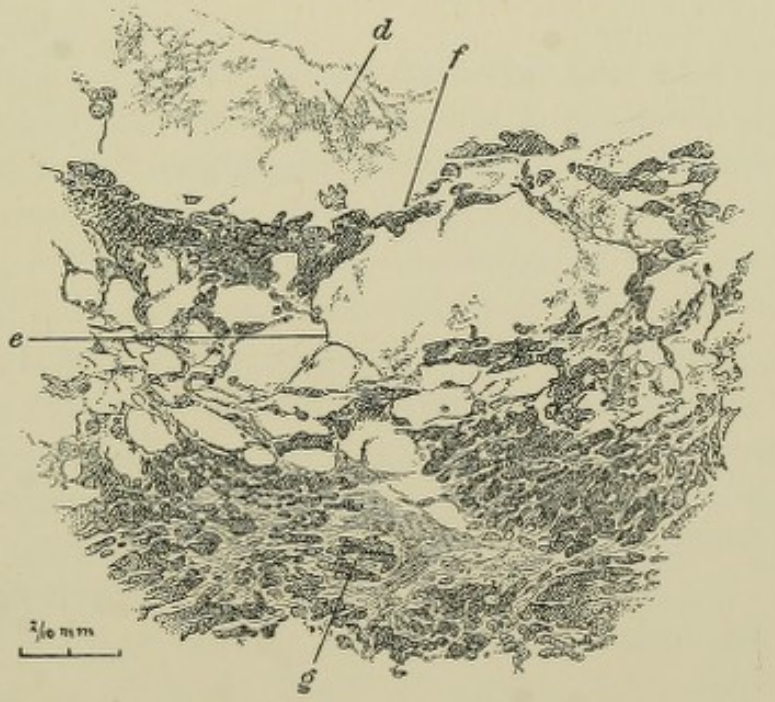


FIG. 79.



it is more reasonable to believe that the cysts in the liver and kidneys had their origin in the blood-vessels than in the hepatic and renal ducts, as is commonly assumed to be the case.

Figs. 78 and 79 represent a portion of the liver from the case of cystic disease under discussion. The patient was a man seventy-seven years old who had lived an irregular life and was a hard drinker. The low-power drawing shows the size of the cysts and that they were very numerous. The details of structure are better seen in the picture drawn with greater amplification. This shows the amorphous and shreddy nature of the material which was contained by some of the cysts, and that their walls were made up partly of fibrous tissue, sometimes mere fibrous threads separating one cavity from another, and again that the liver cells themselves constituted the cyst-walls. The columns of liver cells are seen in places to have been flattened by the pressure of the growth of the cysts or of the fibrous tissue, or of both. An important point to be noticed is that there has been an extensive growth of morbid fibrous tissue, and it should be remembered that fibrosis seems to be an invariable accompaniment of cystic disease of the liver. In hepatic fibrosis it is common for the fibrous tissue to form in such a way as to surround a group of the secreting cells, so that the appearance is of an island of liver cells surrounded by the sweeping lines of morbid fibrous tissue. This appearance is never seen in natural liver. Such an island is included in the drawing (Fig. 79).

Figs. 80, 81, 82, and 83 are from the liver of a man forty-seven years old who died of the disease which has been named Charcot's hypertrophic cirrhosis of the liver. The peculiarities of this disease are the growth of fibrous tissue, the enlargement of the liver, which is sometimes very great, and the formation of new bile-ducts. In the case under discussion the liver was fibroid and enormously enlarged, and it presented the appearances which are commonly considered to denote the formation of new bile-ducts. The pictures upon the plate show these well-known lesions, but they also demonstrate the existence of other pathological lesions which are usually supposed not to have any relation to the disease. Their study is both interesting and highly instructive.

Fig. 80 is a cyst surrounded by fibrous tissue. At one side in its wall there was a deposit of calcareous material,—very well shown by the drawing. The cyst was sufficiently large to be easily seen with the naked eye, and was surrounded with yellowish, degenerated mate-

rial. It lay quite close to the capsule of the liver, and in fibrous tissue which had grown directly under and was continuous with the capsule. This morbid fibrous material presents an open-meshed appearance, the holes being so large as to suggest that the tissue was all in such a condition that there was a tendency to the development of numerous cysts. Another cyst is included which is very minute, and its peculiarities (see description of plate) are better shown by Fig. 81, which exhibits it more highly magnified. It must be a very early stage of cyst development, for the cavity is subdivided by numerous partitions, which appear as fine threads in which are a few cell-nuclei. How cysts originate is an interesting question, but one which cannot be answered. The minute threads which run across the cyst, and which are, of course, only the cut edges of thin membranes subdividing the cyst into numerous chambers, are structurally similar to the endothelium of the walls of capillaries. It is very common to find cysts of considerable size, notably in the kidney, which are divided or partly divided by membranes or membranous shelves. The fact that the partitions in this minute cyst are so like endothelium suggests again the question of the influence of capillaries in the production of cysts, and whether in this case also they had their origin in the capillaries.

Fig. 82 represents one of the so-called new-formed bile-ducts. The picture is of tissue near the capsule, and it is very common to find the new ducts in this region, and even lying in the thickened capsule itself. This is to be explained, perhaps, by the fact that fibrous tissue is very apt to grow in the neighborhood of, and in connection with, the capsule of the liver in cirrhosis. The duct is seen to be composed of cells like epithelium, which are arranged in an irregular double row, and it is forked two or three times. It lies in fibrous tissue, no liver cells nor anything that would enable one to recognize that it is liver being included. This forking column of cells, which is a fair type of the so-called new bile-ducts, has nothing in its appearance that is like the ordinary bile-ducts in human liver. The cells do not resemble in the least the peculiar columnar cells that line bile-ducts. The column of cells in the picture does, however, recall to mind strongly the appearances sometimes presented by developing ducts in embryological tissues. In this resemblance to developing ducts in embryos is found the only reason why such columns of cells, which are always very numerous in hypertrophic cirrhosis, are looked upon as new bile-ducts.

Fig. 83 presents an appearance which has confirmed me in the

FIG. 80.—CYSTIC DISEASE OF THE LIVER. (× 12.)

From a man of forty-seven years who died of cirrhosis of the liver of the form sometimes called the hypertrophic cirrhosis of Charcot; the section was taken from a fibrous region near the capsule. The central space is a cyst large enough to have been seen with the unaided eye; surrounding it is fibrous tissue which in the immediate neighborhood of the cyst is torn and in which some mineral substance (*m*) was deposited. *a* is a very minute cyst, represented more highly magnified in Fig. 81.

FIG. 81.—CYSTIC DISEASE OF THE LIVER. (× 55.)

The cyst *a* from Fig. 80, more highly magnified. It is surrounded by fibrous tissue which is rich in nuclei; across the cyst-cavity are stretched very numerous fine threads in which there are a few nuclei. These threads were membranous partitions which subdivided the cyst-cavity into very many minute spaces.

FIG. 82.—RETROGRESSION OF LIVER TISSUE. THE SO-CALLED NEW BILE-DUCTS. (× 280.)

From the same case of Charcot's hypertrophic cirrhosis as Fig. 80. The picture represents in a typical manner one of the branching collections of cells lying in new-grown fibrous tissue which it is usual to describe as developing bile-ducts.

FIG. 83.—RETROGRESSION OF LIVER TISSUE. (× 280.)

From the same tissue as Fig. 82. There is liver tissue in which there are many cavities exactly like those described as a form of cyst in Figs. 74 and 75; they are usually very numerous in cases of hypertrophic cirrhosis. *f* is fibrous tissue. *d* would probably be commonly described as a developing bile-duct. To the left it is composed of a closely packed collection of small cells which are arranged in a double row, while at its right-hand end, where it is broadest, its appearance is exactly that of somewhat degenerated liver cells with invisible or very shadowy nuclei. The appearance suggests the explanation that what was once a trabecula of liver cells has been compressed by the growing fibrous tissue until it assumed the condition described and depicted.

2/10 mm.

Fig. 81

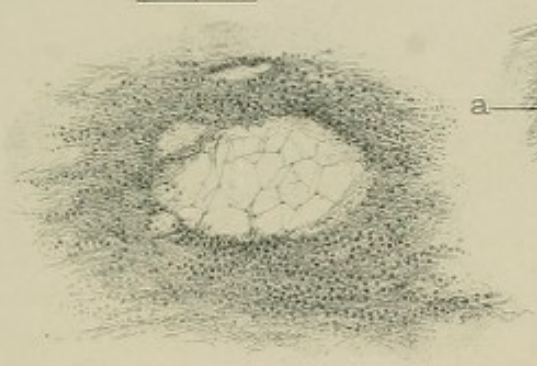


Fig. 80

1 mm.

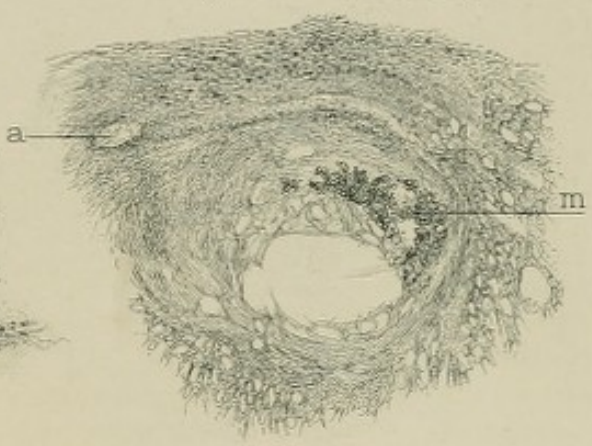


Fig. 82

5/100 mm.

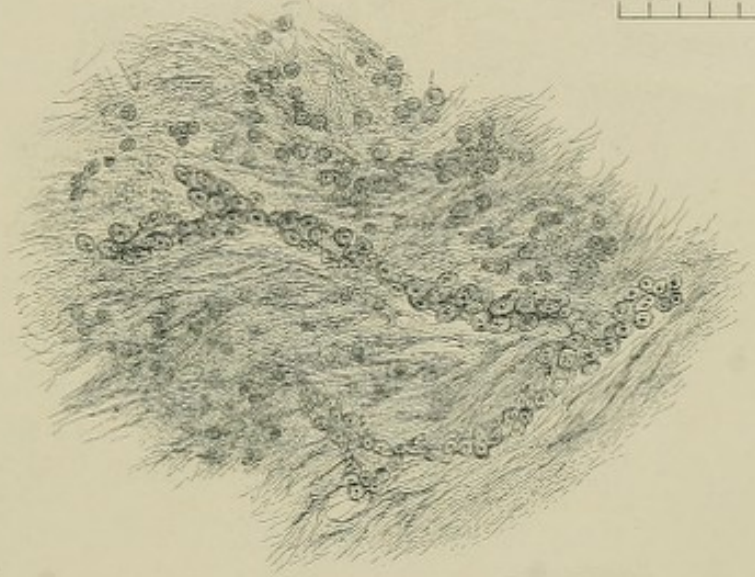


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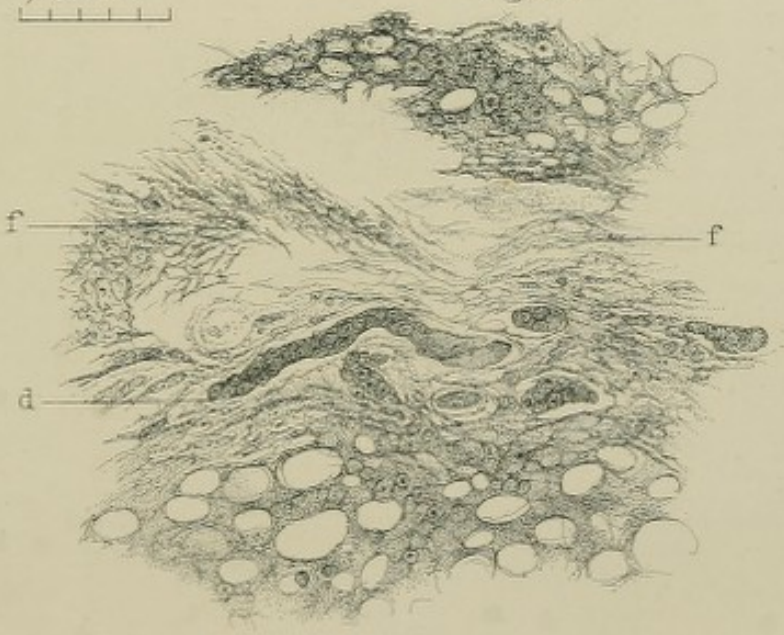
Fig. 83



opinion I held before I ever saw this particular section, that the so-called new bile-ducts the formation of which is the most pronounced feature of Charcot's hypertrophic cirrhosis of the liver are not bile-ducts; and that the common explanation of their presence is erroneous. In mammalian embryos the liver is a very large organ developed from the alimentary canal. At first there are ducts which become more and more complex, then the columns of liver cells appear. It may almost be said that the trabeculæ of secreting cells are developed from the bile-ducts, or, if this is not considered to be exactly the case, it is certainly true that liver cells appear after bile-ducts have been formed and in direct connection with them. Upon examination, the theory that nature forms a vast number of new bile-ducts in hypertrophic cirrhosis of the liver, which is a process of destruction, seems a strange one and most unlikely. There is not known in human pathology any other instance of such useless development. Why should bile-ducts grow in vast numbers in a liver undergoing rapid destruction? It has already been suggested by Goodhart* that there is no growth of new ducts in hypertrophic cirrhosis, and he quotes from others in support of this. Fig. 83 shows a column of cells which aids to prove the view to be correct that the process is one of retrogression, that the trabeculæ of liver cells, owing to the pressure to which they are subjected, or to mere shrinkage in process of degeneration, become changed into columns of cells of the kind which have been supposed to be new bile-ducts. This particular column of cells (*d*, Fig. 83) has at one end the appearance of a so-called new bile-duct, being composed of a double row of closely appressed epithelial cells, and at the other end it is made up of secreting cells. The drawing does not, of course, show this so well as the object itself when it is examined with the microscope and the different parts are accurately brought into focus and the details studied. The exhibition of the transition of a liver trabecula into a duct, a thing quite unknown in healthy liver, does not seem susceptible of any other explanation than that the process is one of retrogression or involution, the cells changing and shrinking to return nearly to their primary embryological state. A change parallel to this may occur in the kidney in fibrosis, a renal tubule being compressed until it looks very like *d* in Fig. 83. Such a condition is illustrated by Fig. 116. The fact that the squeezing by fibrous growth

* New Sydenham Society, Atlas of Pathology, Fasciculus iv.

produces very similar appearances both in the liver and in the kidney strengthens the view that it is a retrogressive change in the direction of the embryological condition. The drawing shows also that the liver was full of holes similar to those already described. Such spaces are in my experience invariably present in cirrhosis, and especially in hypertrophic cirrhosis, of the liver, and it does not seem possible that they are only the result of ordinary fatty degeneration. The number of these spaces is often very great. In one case in particular, of a woman who died with a liver weighing thirteen pounds, which was very hard and did not feel or look in the least oily, it was difficult with the microscope to recognize the tissue as liver. The appearance was that of innumerable holes surrounded by fibrous walls, which were much thicker than the usual envelopes of fat-globules; only here and there after careful search could a few characteristic cells be found to betray that the tissue was liver. In another case, of a boy of seventeen who died of hypertrophy of the heart and in whom the pericardial sac was obliterated by inflammatory adhesion, a chemical analysis to test the amount of fat was made for me by Professor John Marshall. When dried, the liver was found to contain forty-six per cent. of oil. In normal dried liver the amount of oil is ten and one-half per cent. This liver was noted at the post-mortem examination to be "exceedingly enlarged, not greasy, remarkably mottled." When examined with the microscope, it seemed to be a mass of holes and little else. The amount of oil as shown by the analysis was little more than four times the normal, while the microscopical appearance of the tissue was such as to make it seem that the percentage must have been at least eighty or ninety if all the holes had been filled with oil. The process has been described as vacuolation, and perhaps it is this form of degeneration that is meant by "cavernous metamorphosis," but no satisfactory explanation of these diseases has been suggested. The conclusion to which I am driven is that the commonly accepted theory that these holes are all the result of fatty degeneration is inadequate to explain the disease. It has already been suggested that the process is an early stage of cystic disease. In the vast majority of cases, however, they never become sufficiently large to be distinguishable with the unaided eye.

Figs. 84 and 85 represent the appearances of ordinary contracting cirrhosis of the liver, or, as it is often named, Laennec's cirrhosis. The first of them is from the liver of a woman of sixty who died of Bright's disease with extensive fibrosis of the heart, spleen, and kid-

FIG. 84.—CIRRHOSIS OF THE LIVER. (× 46.)

From a woman sixty years old who died of Bright's disease. It is typical of cirrhosis: there are islands of liver cells surrounded by broad bands of fibrous tissue. At *j* the fibrous tissue and blood-spaces are greatly increased in bulk, while the columns of cells are attenuated, being in process of extinction. The whole island was being rapidly extinguished. The capsule is indicated by *f* and *g*, which denote respectively the outer free surface and the under surface. In this section no distinction can be made between the capsule and the fibrous bands extending downward into the liver, for they are identical in structure and continuous one with the other. Fig. 85 presents a striking contrast in this respect.

FIG. 85.—FIBROSIS OF THE LIVER. (× 48.)

From a man fifty-seven years old who died of Bright's disease. To the right in the drawing (*e*) dense fibrous tissue bands extend into the liver and are continuous with the capsule, which is of similar structure with and indistinguishable from the bands. In this respect the appearance is the same as in Fig. 84. To the left in the drawing the capsule has a different appearance. *f* is its upper and *g* its lower surface. Upon it has grown a fibromatous deposit. *u* with its diverging lines indicates the thickness of this, and underneath this region the thickened capsule merges into the liver substance so that there is no line of demarcation between them, and the fibrous capsule is evidently growing in thickness at the expense of the liver. Under the fibroma the capsule is depressed. *d* is a fibrous band extending into the substance of the liver. The columns of liver cells have been made thin by pressure.

FIG. 84.

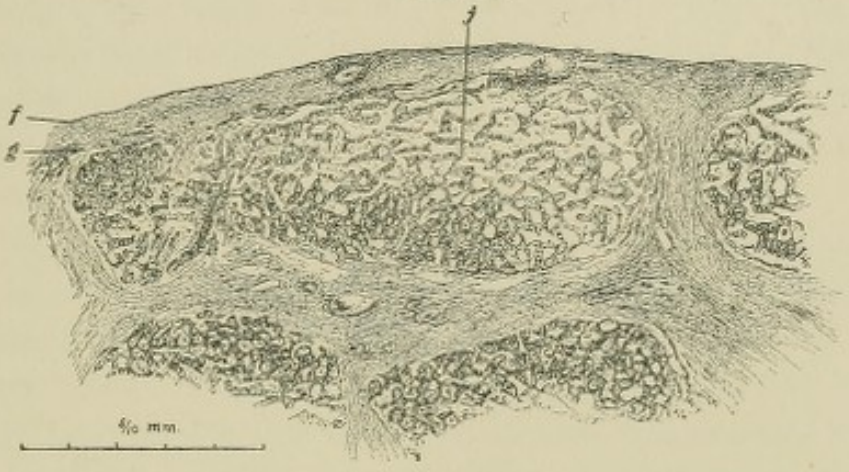
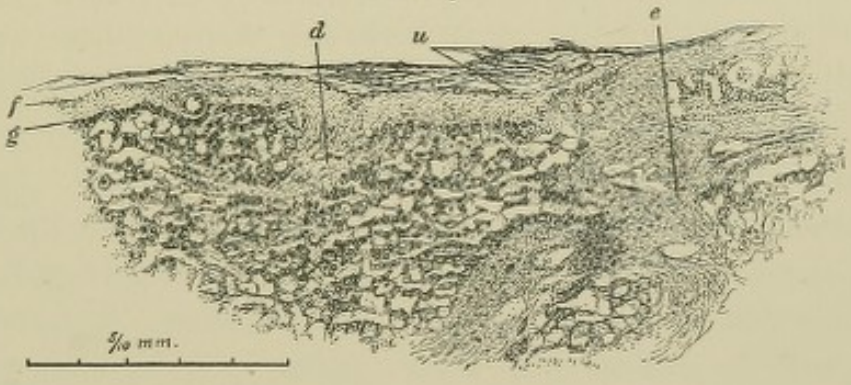


FIG. 85.



neys, as well as of the liver. There are islands of liver surrounded by broad bands of fibrous tissue; the columns of secreting cells in the islands are narrow, are in process of destruction, and the blood-spaces are enlarged. It is probable that the true liver skeleton, the fine but strong fibrous framework in which the columns of secreting cells are held, undergoes increase as a part of the general process of fibrosis. The persistence of this framework in nutmeg liver in portions of the organ from which all trace of the secreting cells has disappeared has been mentioned (page 104). In the present case the thickened capsule of the liver is continuous with the fibrous bands which ramify among the liver islands, and is of exactly similar structure, so that it cannot be said where the one ends and the other begins. Fig. 85 is from the liver of a man of fifty-seven who died of Bright's disease. He had extreme fibrosis of many of the organs and of the arteries, and much calcareous material had been deposited in the tissues, organs, and arteries. The cirrhosis was of less advanced stage, and the morbid fibrous tissue, being of recent formation, is more cellular and less purely fibrous than in the first case. It is also less sharply separated from the liver substance, the two merging at their junction instead of showing a sharp line of demarcation. The capsule of the liver is thickened, and in a part of the tissue represented it is continuous with bands of fibrous tissue which have penetrated into the liver substance. In another part, the capsule although decidedly thicker than natural is made up of distinct fibres to a much less degree and merges into the liver substance beneath, so that there is no line of separation, and at this place it shows how fibroid tissue is growing at the expense of the liver. A characteristic feature of the process is the growth of fibrous material upon the surface of the capsule. This is very common in the liver, but even more so in the spleen (page 116). Such fibrous growths sometimes take the form of minute fibromatous tumors, or, as in this instance, it may be only a small amount of loose-meshed material of coarse fibrous strands containing scattered cells. A fibrous growth of this nature upon the surface of the capsule usually forms for itself a depression in which to lie, and such is the case with this one. The shrinkage of the fibrous tissue pulling at its attached ends draws the capsule over it as a bow is drawn by the string, and thus the fibrous growth sinks in the softer substance beneath it. It is very common to find many of the so-called new bile-ducts in cases of cirrhosis of the atrophic as well as the hypertrophic form. In fact, all the histological features which have been

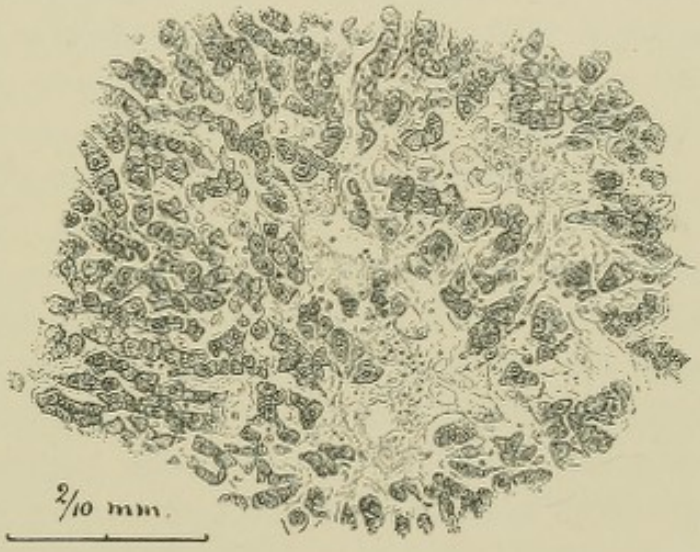
supposed to be peculiar to hypertrophic cirrhosis are to be found in the contracting form.

Fig. 86, which is from the liver of a man of forty-eight who died of dysentery, illustrates an early stage of hepatic fibrosis. Fibrous tissue has developed in the midst of the liver substance, and the appearances seem to indicate that the theory which was advanced long ago that the liver cells themselves are converted into fibrous tissue is correct. It appears as if some of the secreting cells were undergoing such a transformation. The picture shows also what seems to be an increase of the fine fibrous framework. The framework of the liver is like a complicated system of fine tubes into the interior of which the liver cells are packed in columns. The fact has already been mentioned that this framework or skeleton is very persistent and of considerable strength, for it often preserves its form unchanged in cases of nutmeg liver after the liver cells themselves have entirely disappeared. It has been disputed in the past whether there is any fibrous tissue in the liver except that of Glisson's capsule, but it would be impossible for any one after examining sections of nutmeg liver from which the secreting cells have disappeared to doubt that there is a supporting frame to hold the cells in their positions, and that this frame is of different structure from the cells themselves. There can be no doubt that the growth due to disease of this fine framework goes to form part of the masses of fibrous tissue that are found in the liver in cirrhosis, and it is probable that the liver cells themselves by some process of conversion or of retrogression contribute toward the fibrous formation. The question of the origin of cirrhosis is an important one, and it is most likely that the view is correct that the first visible sign of it is an increase of the number of the nuclei of Glisson's capsule in the portal channels. The illustration exemplifies the fact that in any particular disease it is very common to find other pathological lesions besides those which are peculiar to it, and sometimes in organs in which they would be least expected, if they are carefully sought. In this case the patient died of dysentery, and there is every reason to suppose that the hepatic fibrosis was of older date than the dysentery. Whether such fibrosis of organs is harmless or becomes the seat of origin of disease is a most important point in a general question of vast extent. It is certain, however, that such fibroid changes are sure to come in the organs of all people if life is sufficiently prolonged. In some the change is late, and in others it is early. It is apt to begin early in those who have suffered with chronic

FIG. 86.—FIBROSIS OF THE LIVER IN SCATTERED SPOTS. (× 90.)

From a man of forty-eight years who died of dysentery. The increase of fibrous tissue is very plain, and it is certain that it is the result of disease, for the area depicted is not near any portal vein, around which there is always fibrous tissue.

Fig. 86.



disease, and to be found in persons who have the appearance of premature age.

Fig. 87 represents a curious form of disorganization and fibrosis of the liver. It is from a woman thirty years old who died of an irregular form of Bright's disease after having had persistent vomiting for several weeks. The natural arrangement of the liver cells in columns is entirely lost. They lie irregularly scattered each by itself or two or three together, and the intervals between the cells are filled with a fine, almost structureless material. Such a condition is difficult to explain. There were degeneration of the heart (Fig. 53), two minute aneurisms in the aorta (Figs. 30, 31, and 32), fibrosis of the spleen and kidneys, and a peculiar degeneration of the stomach (Fig. 103), besides the disease of the liver. It seems as if the fibrosis and subinflammation which are of such frequent occurrence in old people and come on so slowly that the organism has time to become accustomed to them and acquire the power to bear them had in this instance come rapidly in a woman only thirty years old,—that old age had come upon her with such speed that it killed her suddenly.

Two notable conditions are illustrated by Fig. 88, which is from the liver of a man of twenty-seven who died of acute cholera morbus. There are a number of spaces within liver cells. These would probably be called by most pathologists vacuoles, but to say that such an appearance is the result of vacuolation is only to name a thing which is neither described nor explained. If there really be such a process as vacuolation, it must be a miniature form of cystic degeneration, and the appearances here depicted bear out this view. The cavities are surrounded by distinct walls, as is usually the case with small cysts, and there is a little fine structureless material lying within them. The second point of interest illustrated by the drawing is the demonstration of other disease besides lesion of the intestine in a case of acute cholera morbus of a duration of only about forty-eight hours.

In the liver, as in all other parts of the body, it is very common for the blood-vessels to be diseased. Those most commonly affected are the branches of the hepatic artery, the walls of which become thickened in every possible degree, from the slightest increase of the intima to total closure of the vessel by endarteritis obliterans. The other vessels also are liable to disease, the portal veins being frequently affected, but in my experience disease of the hepatic veins of such degree as to attract attention is not very common. Disease, therefore, is most frequent in those vessels which have in proportion to their

calibres the thickest walls and are surrounded by connective tissue, —the hepatic arteries,—and least frequent in those of which the walls are thinnest and which are without connective tissue around them,— the hepatic veins. With regard to blood-vessels in the liver, it is a curious fact that in cirrhosis even of the hypertrophic form with great enlargement there is apparent paucity of vessels, the liver being hard, woody, nodulated, and tough on section. The fact was mentioned in connection with the subject of hepatic cirrhosis that what have been called new bile-ducts are often to be found in the capsule. These ducts are frequently present in the thickened capsule of the liver in cases of Bright's disease, and were found by me in a case of associated Bright's disease and phthisis, in which the degree of fibrosis of the liver was so slight that no one would have said there was cirrhosis if the specimen had not been examined with the microscope. The association of Bright's disease in which there is hepatic fibrosis with consumption of the lungs is of such frequent occurrence that it makes one think there must be some relationship between the diseases, and in malignant disease of the liver the microscopical lesions of cirrhosis are sometimes so intimately associated with the new growth that their satisfactory separation is impossible, and the mind is driven to the conclusion that the processes are by no means so far apart as is ordinarily taught. In tuberculosis of the liver more than of any other organ giant cells are apt to be found in typical form, and in the liver, as in other organs, it is occasionally impossible to distinguish between miliary tubercles and miliary abscesses. The secreting cells of the liver often present peculiarities the study of which is certain some day to result in the acquisition of knowledge which will aid in the comprehension of disease and in its cure. There cannot be any doubt that the number of the secreting cells often increases in disease and that the liver thus becomes enlarged. One of the commonest microscopical appearances of the cells is an exaggerated prominence of the nuclei, so that they produce a staring effect in stained sections, in diseases accompanied by active inflammation or by exaltation of the circulation in the earlier stages. In such cases, and especially in one case of malignant disease within the portal vessels, I have seen the nuclei in process of fission. Such cells, if preserved more perfectly than can be done with pathological tissues, would almost surely have shown the various karyokinetic changes. It has been said that cirrhosis of the liver probably has its beginning in an increase of the number of nuclei in the portal channels; but hepatic fibrosis at an early stage

FIG. 87.—DISARRANGEMENT OF THE CELLS OF THE LIVER AND FIBROSIS. (× 105.)

From a woman thirty years old who died of Bright's disease, having had persistent vomiting for several weeks. The arrangement of the cells in columns has been destroyed; they are scattered singly and in disorder. There is an increase of fibrous tissue.

FIG. 88.—DEGENERATION OF LIVER CELLS. (× 220.)

From a man of twenty-seven years who died of acute cholera morbus. *c* indicates cells which have within them spaces which are empty or contain some amorphous material. Such spaces are surrounded by a distinct ring. *h* is a small blood-vessel cut longitudinally and containing corpuscles.

FIG. 87.

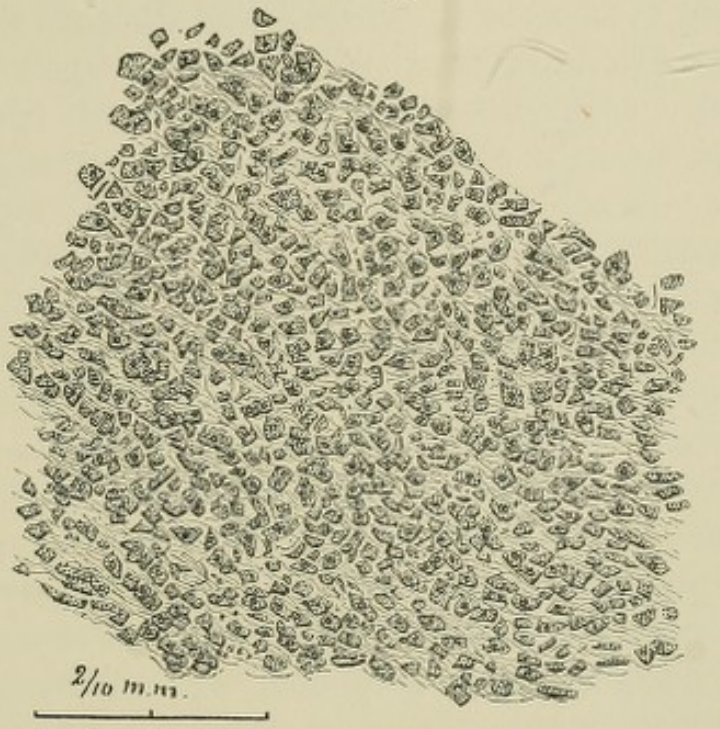
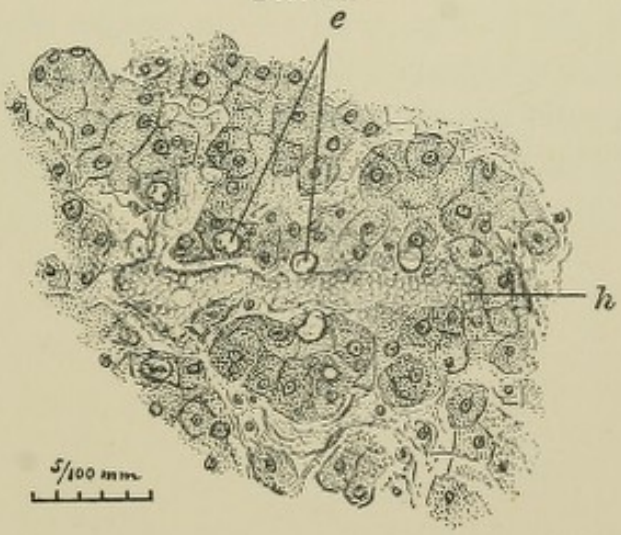


FIG. 88.



occasionally assumes strange forms, and the acini are sometimes surrounded by fine fibrous tissue in such a way that the liver resembles that of the pig. Amyloid disease of the liver, like amyloid disease of other organs, has long remained a pathological puzzle. It does seem, however, that it must be closely connected with the fibroid process, or even one of its forms. The consideration of disease of the liver both clinically and from the stand-point of gross and microscopical pathology has convinced me that existing classifications are inadequate and unsatisfactory, because they give a false impression that many diseases which are related or parts of one process are entirely separate from one another. There can be no doubt, for instance, that cirrhosis is only the result of inflammatory and cellular growth of a character similar to that which may take place in other parts of the body, and therefore that whether the liver is enlarged or reduced in size the disease is the same one with variations. As a pathological process it is often on the one hand but little removed from hypertrophy, and on the other approaches closely to malignancy or tumor growth. The relation of tuberculosis to these diseases is sometimes very close and the lesions are hopelessly entangled. If all these diseases were known to be merely modifications of growth, the pathology of the liver would be much simplified, and it would no longer be necessary to fit in an extraneous material cause, as it is commonly believed must be done in cancer and tuberculosis. It is important never to forget that morbid fibrosis constitutes an essential part of all chronic disease of the liver, and at the same time that the increase of fibrous tissue is a natural consequence of age in the human body. To estimate justly the influence of the natural processes of age and of chronic disease is often very difficult, if not impossible.

CHAPTER VIII.

THE SPLEEN.

The spleen is an organ of unknown function, but there is every reason for believing that it plays an important part in the economy. It is certain that its liability to disease is very great, and that it is often diseased early in life. As early as the fifth or sixth month the spleen will sometimes be found to be pigmented and unnaturally fibroid, with thickened capsule and trabeculæ, and diseased vessels, in persons dead of chronic disease. There is no organ which shows more certainly the increase of years, as in older persons it becomes more dense and fibrous and the vessels thicken. These changes due to the advance of years may be concealed in persons who have died of diseases which occasion enlargement or softening of the spleen. The most frequent lesion, perhaps, in chronic disease is thickening of the capsule. The spleen capsule is, if possible, more liable to disease than the capsules of other organs, and adhesion to surrounding parts is of very frequent occurrence.

Fig. 89 is from the spleen of a man of fifty-seven who died of Bright's disease, and it represents thickening of the capsule in an extreme degree, but in a form that is very common. The natural capsule remains apparently unchanged, and upon its outer surface has been developed a layer of coarse fibrous tissue of very varying thickness. The effect has been to force the capsule downward in some places into the splenic pulp. The fibrous tissue in this case has developed separately and constitutes a tumor grown upon the capsule. The two layers are distinctly shown by the drawing.

Fig. 90 shows a form of fibrous growth which is of frequent occurrence. It is a true fibroma, a tumor developed upon the surface of the capsule. These growths are in my experience very common in persons past middle life who have died of chronic disease, and they present themselves as minute seed-like protuberances upon the surface of the organ. Such a growth I once found as early as at ten years, and the spleen was fibroid and the vessels thickened. The patient died of chronic disease of the heart. They are white and opaque in most instances, the capsule is generally thickened and whiter than

FIG. 89.—FIBROMA OF THE SPLEEN. (× 11.)

From a man of fifty-seven years who died of Bright's disease. The true capsule is seen as a membrane of even thickness, upon the upper surface of which is the new-grown fibroid tissue constituting a layer of very varying thickness. The splenic pulp is below.

FIG. 90.—SMALL FIBROMA OF THE SPLEEN. (× 11.)

From a man of fifty-one years who died of perihepatic abscess. The capsule is of nearly even thickness, and the fibrous prolongations from it into the splenic pulp constituting the trabeculæ are shown. The fibroma is set upon the capsule and sinks it into the spleen pulp: it may be compared to a bow and its string, the curved lines of the capsule underneath being the bow, and the strands of the fibroma the string.

FIG. 89.

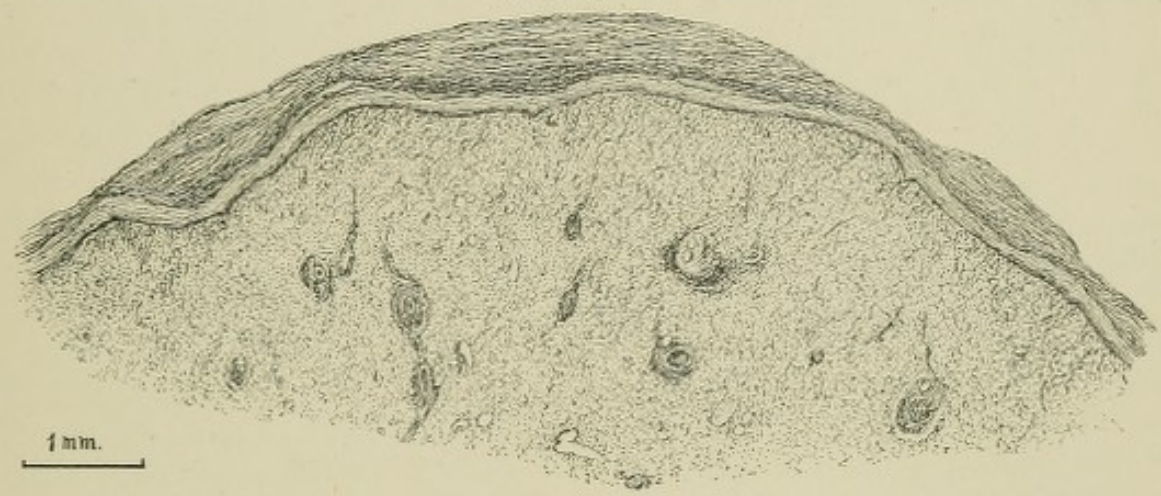


FIG. 90.

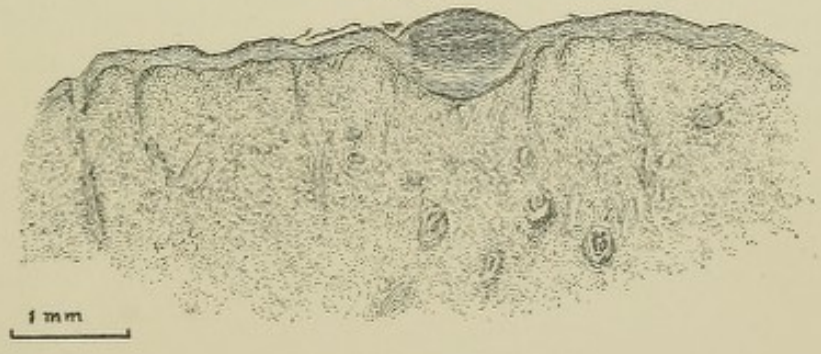


FIG. 91.—FIBROID SPLEEN. (× 11.)

From a woman of sixty years who died of Bright's disease. Through the portion of spleen depicted, from top to bottom there passes a broad band of fibrous tissue. *a* marks its boundary on the left, and *b* on the right. The boundaries are quite sharply marked, and in the band itself there is nothing remaining which is like ordinary spleen tissue. Above, the band widens so as to be somewhat wedge-shaped, with the base of the wedge upward and against the capsule. *c* to *d* is fibroma which has grown upon the capsule; *d* to *e* is the capsule. Both the fibroma and the capsule are depressed at the centre, and they are thrown into two folds. In the depressions caused by the folds there is fibrous tissue which is less dense than most of the fibroma. This was recent growth, and in this manner, partly at least, it must have increased. In all parts of the portion of spleen depicted the fibrous tissue is increased, the trabeculæ are very heavy, and the vessels are thick-walled.

FIG. 92.—FIBROSIS OF THE SPLEEN. (× 220.)

From a negro woman about seventy years old who died of fibrosis of the heart, lungs, liver, spleen, and kidneys. Above is a portion of the spleen capsule. Instead of the splenic pulp's consisting almost entirely of a mass of lymphoid cells, they are sparse and scattered and there are many threads of fibrous tissue. The general effect is that there is not merely a relative increase of fibrous tissue produced by the decreased number of the lymphoid cells, but that the amount of the fibrous elements is absolutely increased. The paucity of lymphoid cells is very striking.

FIG. 91.

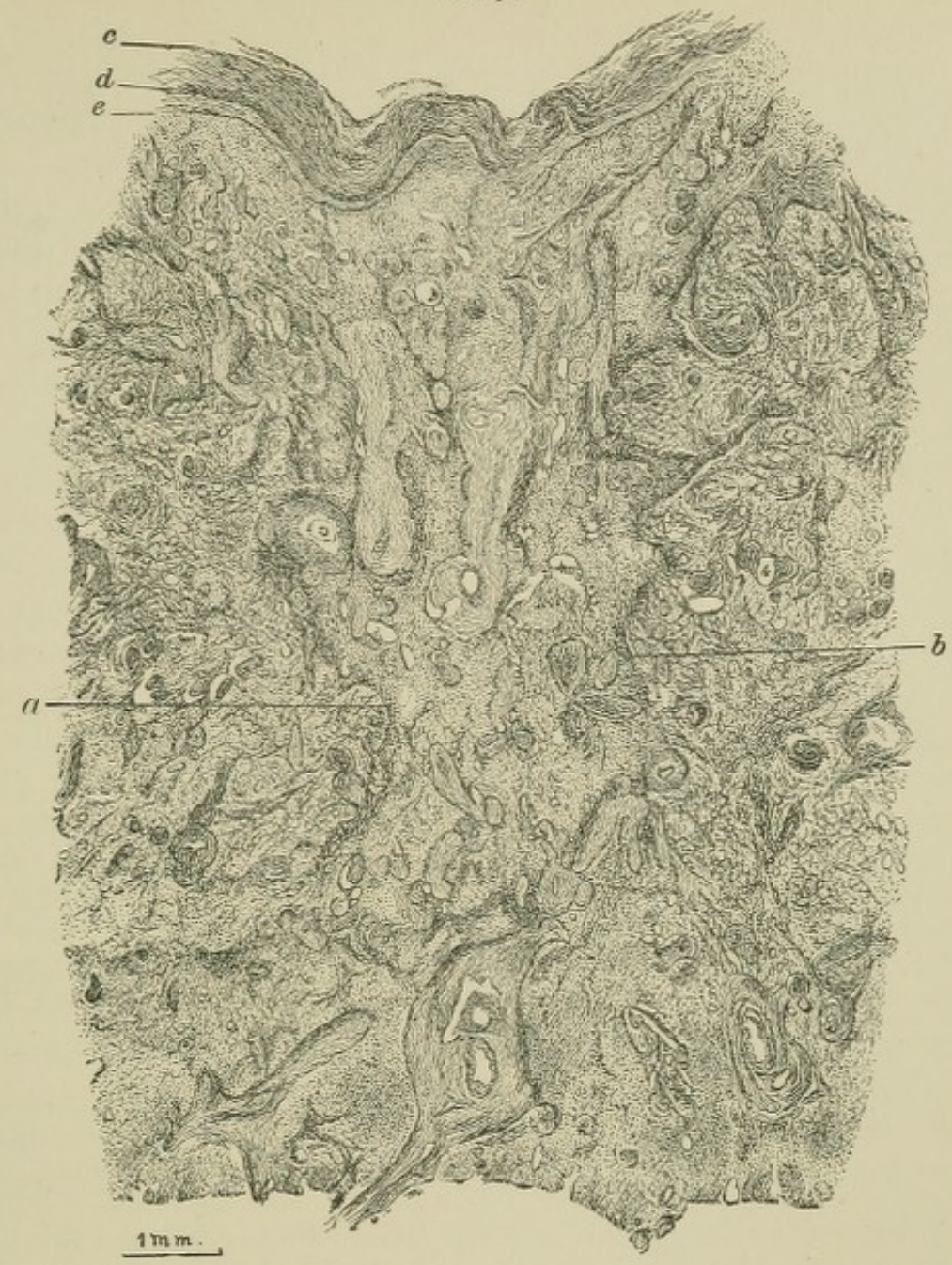
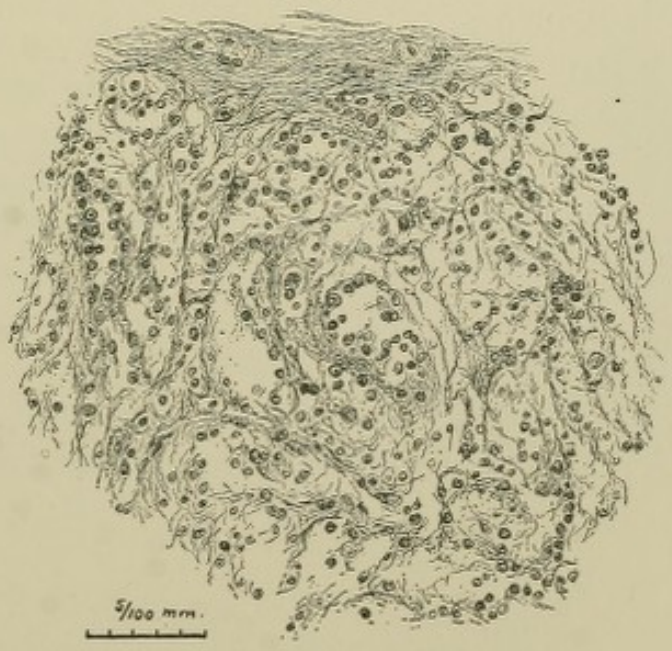


FIG. 92.



natural, and the spleen itself is more or less fibroid. Such fibromatous tumors are often present in considerable numbers. They constitute another evidence of the tendency that exists in older people and in those suffering with chronic disease to an unnatural growth of fibrous tissue, a tendency that has no existence in healthy persons in early life, when the tissues and organs are all soft and pliable.

Fig. 91 is from the spleen of a woman of sixty who died of Bright's disease, and who had also extreme fibrosis of the heart, lungs, and liver. It illustrates splenic fibrosis of the most extreme form. This spleen was rather smaller than natural, the capsule was very white and irregularly thickened, and on section the pulp was hard and fibroid. The drawing shows that there was no natural spleen tissue left; there are thickened vessels, trabeculæ cut in various directions, and fibrous tissue. Through the centre of the portion of spleen depicted (see description of Fig. 91) there runs a morbid fibrous band from which all trace of spleen tissue has disappeared. Upon the capsule there has grown a layer of coarse and puckered fibrous tissue, which in most places is quite separate from the true capsule beneath, although in one place the two are somewhat run together. Fibrosis of the spleen of some degree is an almost invariable accompaniment of age and chronic disease. In combined Bright's disease and phthisis the spleen is generally fibroid, and in a case of cerebral apoplexy I was struck by the condition of the splenic blood-vessels, many of the minute arterioles being almost closed by obliterative endarteritis. The disease-process which occasioned the cerebral hemorrhage did not confine itself to the brain. Ordinarily when the splenic vessels become thickened from disease they assume a different appearance from that of diseased vessels in other tissues and organs. They lose almost all differentiation into coats, and appear as tubes of nearly homogeneous fibrous tissue with very few nuclei. In the natural condition of the spleen minute arteries lie in the trabeculæ, and when diseased they assume an appearance almost identical with that of the fibrous tissue forming the trabeculæ: so that it is often impossible to determine how much of the fibrous tissue belongs to the trabeculæ and how much to the vessel. The effect produced in section is of a fibrous column solid except for the opening of the vessel in its centre, and this is often very small.

Fig. 92 is from a portion of the spleen of a negro woman of about seventy who died of Bright's disease with fibrosis of the heart, lungs, liver, spleen, and kidneys. The spleen was small and very hard, and

there were thick scars on the capsule. It illustrates a curious phase of splenic fibrosis. Although this spleen was noticed at the post-mortem examination to be very hard, its microscopical appearance would lead one to suppose that it was soft. The drawing represents a tissue made up of fine and delicate fibres and a few scattered leucocytes. Healthy spleen as seen in section with the microscope is composed of masses of leucocytes so thick that the reticulum is almost entirely concealed, and therefore the paucity of leucocytes is the most striking feature of the picture. It is not likely that the tissue would be recognized as spleen, so greatly is it changed. The fact that the organ was very hard proves that there was an absolute increase of fibrous tissue. The woman had been exceedingly feeble for a number of years, and yet she had never had any very decided attacks of illness: so that her death might almost be said to have been from old age, so gradual was the progress of the changes in the organs which were found after death. The microscopical appearance of the spleen tallies well with the life-history and the post-mortem conditions: it looks old and incapable. The increased fibrous framework and the few leucocytes, when considered in comparison with the dense and solid structure of healthy spleen, remind one of the difference between wood which is old and rotten and that which is young.

Fig. 93, which is from the spleen of a woman of forty who died of heart disease, illustrates a curious effect of disease. The spleen has been folded in such a manner as to bring two surfaces of the capsule nearly into contact. This result must have been produced while the organ was being reduced in size after having been swollen. The reduction in size not going on at the same rate throughout the organ, it is easy to conceive how it might have been folded to produce the effect which is depicted. A notable feature is that at several points the contiguous surfaces of the capsule have been bound together by inflammatory adhesions. The capsule is much thickened. To recognize the details of structure greater amplification is required. When this is used, it is seen that the adhesion bands are structurally in many respects similar to the thickened capsule. Both the thick capsule and the adhesion bands contain blood-vessels and unnatural-looking cells of character similar to those which have been described as composing part of the new tissue which grows within blood-vessels. Such a folding as this is probably not in itself a thing of much consequence except so far as it might have been a centre from which inflammation could

FIG. 93.—A FOLDED SPLEEN. (× 11.)

From a woman of forty years who died of heart disease. The organ had been bent over so as to bring two surfaces of the capsule nearly into contact. *i* is the capsule; its two surfaces, where contiguous in the fold, have become adherent by four bands, in the uppermost one of which can be seen a blood-vessel (*v*).

FIG. 93.

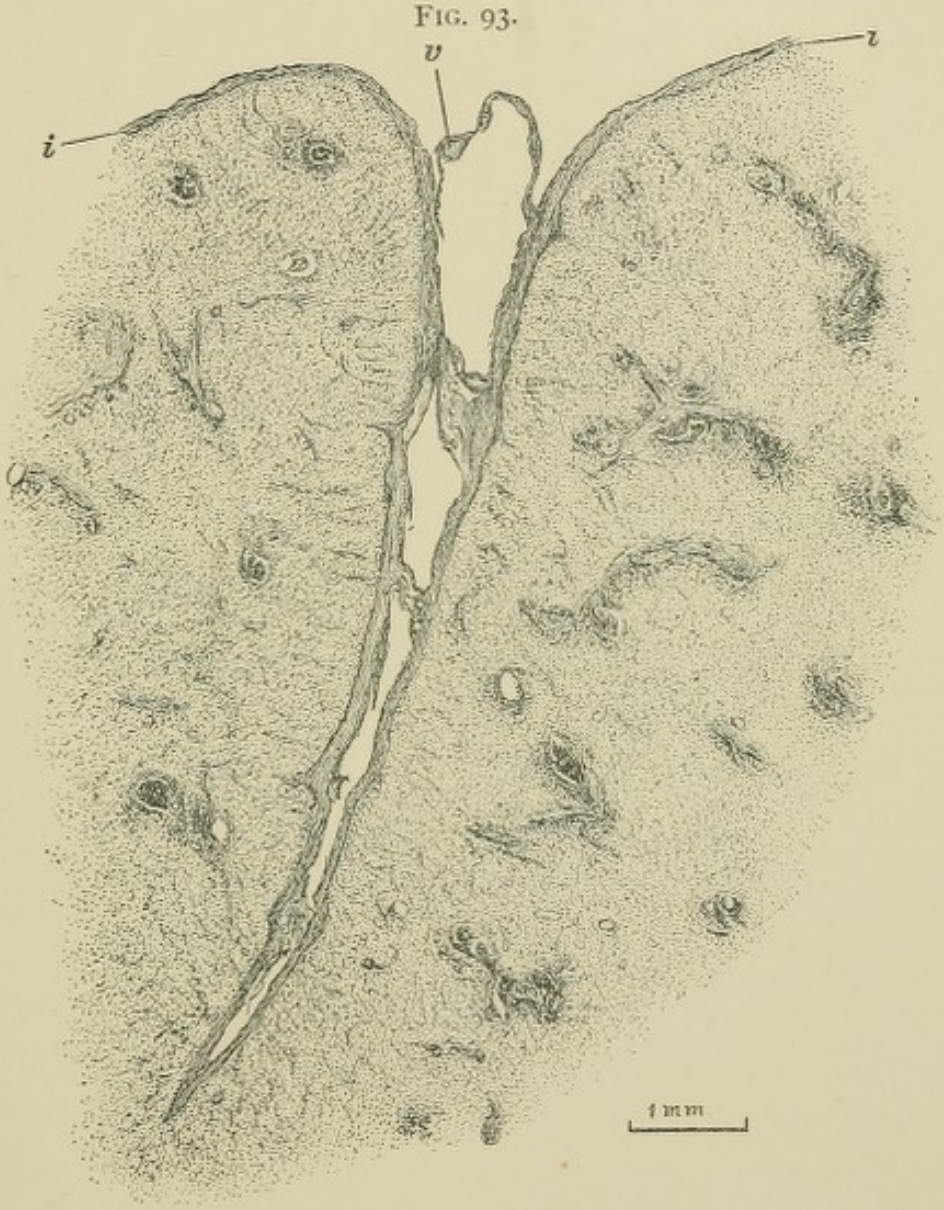
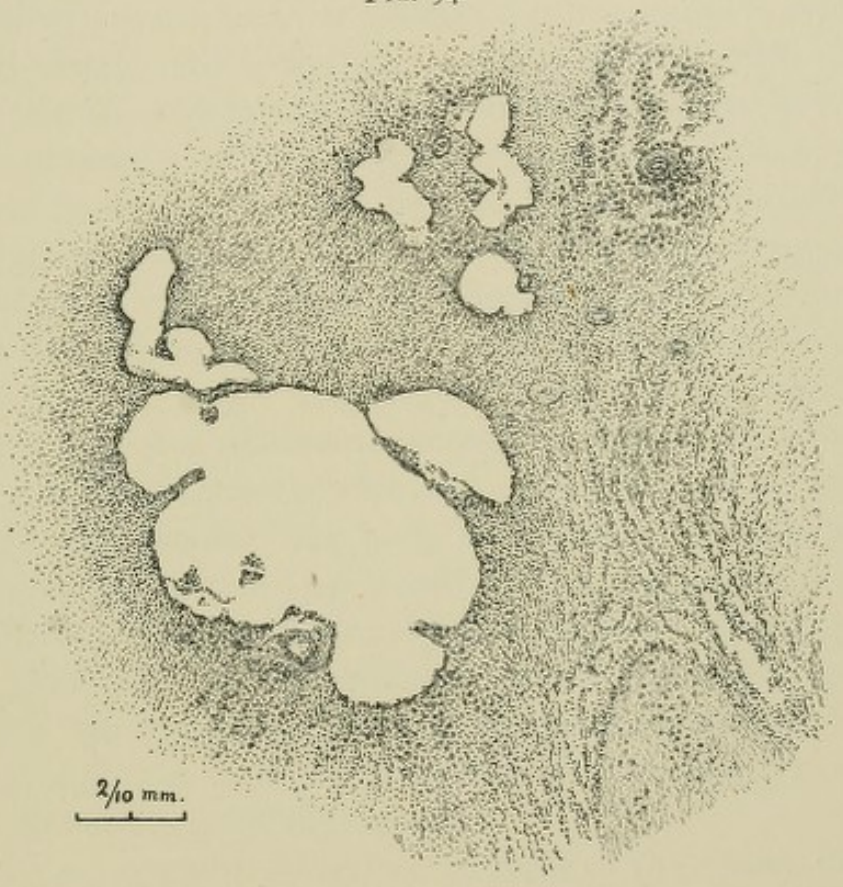


FIG. 94.—CYSTIC SPLEEN. (× 50.)

From a man forty-eight years old who died of heart disease and pulmonary fibrosis. The membranes separating the cysts are in places distinctly fibrous. The arteries are thickened.

FIG. 94.



start. Similar folding and adhesions occur in the liver, but they are apt to be less deep, for the liver is very hard, while the spleen is a soft organ.

In the chapters on the heart and liver it has been shown that cysts are found in the heart, and that they are probably less rare in the liver than is commonly believed. It was suggested that they may originate in the capillaries in the liver, and not, as is generally taught, in the bile-ducts, and it was pointed out that in the heart there are no pre-existing ducts or cavities in which true cysts could arise except the blood-vessels and lymphatics. The same obtains in regard to the spleen: there are no ducts or cavities for true cysts to arise in except the blood-vessels and lymphatics, and, as disease and dilatations of blood-vessels are well known to be common, while comparatively little is known of disease of lymphatics, it would seem much more likely that a cyst in the spleen had had its origin in a blood-vessel than in a lymphatic. Cavities which can be described only as cysts are not rare in the spleen. Fig. 94 represents such cysts in the spleen of a man forty-eight years old who died of hypertrophy of the heart and pulmonary fibrosis. The largest of the cavities is but little more than two-thirds of a millimetre across in its longest diameter, while others are only a fraction of this size. They are all so minute that it is unlikely they would have been seen with the unaided eye. The cyst-walls in this instance are mostly fibrous, and in places there are distinct fibrous threads separating two cavities. As a general thing, cysts of small size have more distinct walls than the larger ones. It seems as if the stretching consequent upon progressive enlargement breaks through the walls, so that the cysts finally are directly surrounded by the tissue of the organ.

Figs. 95, 96, 97, and 98 represent cysts in the spleen of an elderly man who was killed by illuminating-gas poisoning, and who it was found after death had been suffering with pulmonary phthisis and Bright's disease. The patient went with a woman to a room in a hotel, where they must have blown out the gas, for in the morning both were found insensible and the room was full of gas. The woman recovered and walked out of the hospital within twenty-four hours after her admission, but the man never regained consciousness, and in a few days the lungs became congested and he died. It is interesting that the inhalation of an amount of gas that had no serious effect upon a woman who was presumably in good health should have caused the death of a man who had phthisis and Bright's disease. The extensive

chronic disease with which he was suffering had probably been of latent character, so that he did not himself know that he was ill. The case affords an illustration of the fact which has been so much dwelt upon, that acute attacks of illness are often very much affected in their results by pre-existing chronic disease, and that chronic disease may be so latent as to give no sign of its existence. The cysts were of such size that they were easily seen with the unaided eye, and they present a number of points of interest. The accidental discovery of these small cysts in the spleen of a patient who died of pulmonary phthisis and Bright's disease and had also cystic kidneys would seem to point toward some relation of the diseases to one another. It is not likely that the existence of cysts in the kidneys and spleen in the same case was a mere coincidence, but probably they were due in both organs to a single cause. It is remarkable how very commonly fibroid and cystic disease are associated in persons of advanced years, and that some of the forms of pulmonary phthisis which are common in advanced life are found to exist in the same connection. The occurrence of cysts in the spleen is not considered to be common. The cysts illustrated were seen when cut to be filled with a soft, solid substance, which the drawing shows to be composed of granular material intermingled with cells of a character unusual in the spleen. The cells are large and granular, resembling exudate cells, and are in all stages of destruction. It is impossible to know from what portion of the splenic tissue such cells could have been derived, for they are unlike any of its normal cells. A striking characteristic of these cysts is that they all have strongly differentiated walls, in this respect differing from large splenic cysts, which, as will be presently shown, often are simply cavities surrounded by splenic tissue. The walls are formed of bead-like cells which, as is the case with the large exudate cells, are entirely unlike any cells seen in normal spleen.

Figs. 99 and 100 illustrate cystic degeneration of the spleen of great degree. The case was one of cystic disease of the heart, spleen, liver, and kidneys in a man seventy-seven years old, and a report of it has been published.* Illustrations showing the characteristics of the cysts of the heart and liver have already been described. The cavities in the spleen were very numerous, there was great increase of the fibroid tissue, and the blood-vessels were very much diseased and thickened. The cysts have in places distinct fibrous walls, but are generally surrounded directly by the splenic tissue. It is usually the smaller ones

* Journal of Anatomy and Physiology, vol. xxvii. p. 454.

FIG. 95.—CYSTIC SPLEEN. (× 11.)

From an elderly man who died of illuminating-gas poisoning and who was found to have pulmonary tuberculosis and Bright's disease. *c* is the capsule of the spleen. Beneath it are numerous irregularly shaped cysts containing a good deal of solid material. The cavities all have distinct walls. *x* is the cyst represented more highly magnified in Fig. 96.

FIG. 96.—CYSTIC SPLEEN. (× 44.)

The cyst *x* in Fig. 95, more highly magnified. The material within the cavity is composed of granular débris and many large exudate cells. *b* is the upper end of a smaller cavity which also contains some granular substance. The walls of both the cavities are fibrous, and there is at most places a lining membrane containing ovoid bead-like cells. The enlargement is not sufficient to make these cells very distinct; they can be better studied in Figs. 97 and 98. *a* denotes the area represented more highly magnified in Fig. 97; *b*, the area represented more highly magnified in Fig. 98.

FIG. 97.—CYSTIC SPLEEN. (× 280.)

The area *a* in Fig. 96, more highly magnified. The line *r* to *s* corresponds with the line extending from *a* into the cavity of the cyst in Fig. 96. *e* indicates the exudate cells; some of them have a distinct external wall with sharply defined nucleus and granular contents, others are in various stages of destruction, the nuclei melting down, the walls gone, and the cells running together to become mere masses of structureless granular débris. *w* is the wall dividing the large cyst from the small one; its central portion consists of fibrous tissue, and upon each side are the membranes containing ovoid bead-like cells (*c*) which formed the lining of the larger and smaller cysts. *z* is a portion of the wall to the right of the smaller cyst.

FIG. 98.—CYSTIC SPLEEN. (× 280.)

A free-hand sketch of the upper portion of the smaller cyst in Fig. 96 and indicated by *b*. Drawn with the same amplification as Fig. 97 and to correspond with it in size. In the lower part of the picture the cyst-walls have been cut sharply across, and the bead-like oval cells in the lining membrane are distinct, while in the upper portion the plane of section has been somewhat sloping, cutting the cells across in such a manner that they look like somewhat disarranged epithelium.

Fig. 95

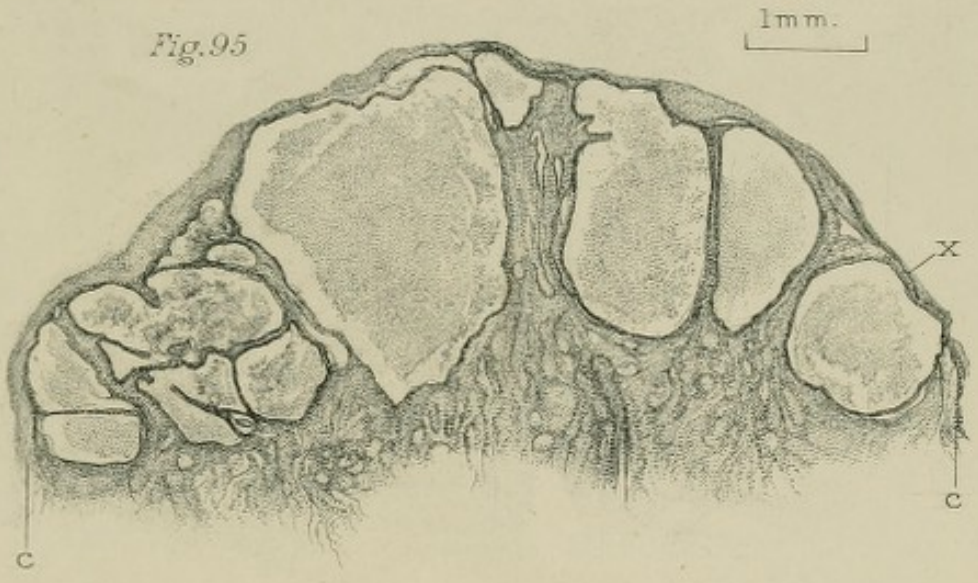


Fig. 96

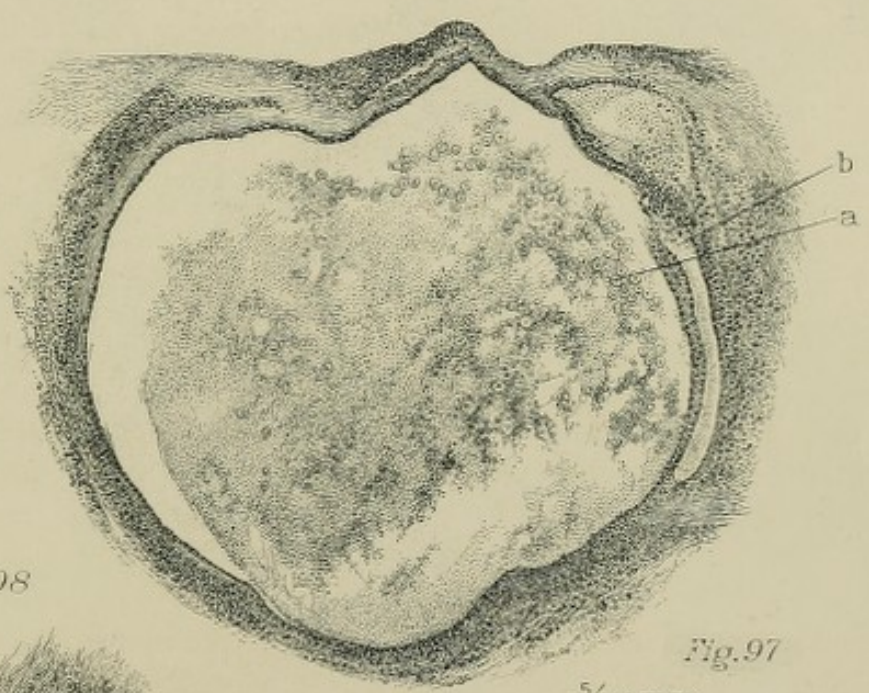


Fig. 98

Fig. 97

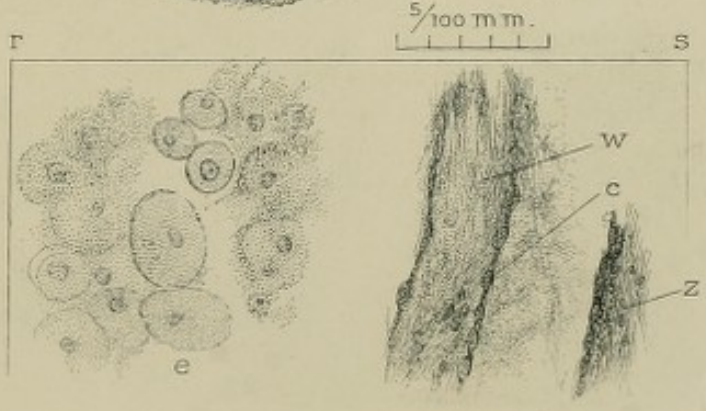


FIG. 99.—CYSTIC SPLEEN. (× 6.)

From a man of seventy-seven years who had also cystic disease of the heart, liver, and kidneys. *c* is the capsule. The cysts are of various sizes, and some have a fibrous cyst-wall and others are without any. *d* is a fibrous cyst-wall. *e* denotes a portion of the section torn in preparation (not a cyst). *k* is the area shown more highly magnified in Fig. 100.

FIG. 100.—CYSTIC SPLEEN. (× 50.)

The area *k* in Fig. 99, more highly magnified. *t* is a trabecula. There are several cysts included: some contain structureless solid material, others are empty. Around the cysts there is no fibrous wall, the spleen-pulp constituting their boundaries. *l* is fibrous tissue which was broken in process of preparation: it was part of a cyst-wall. Two minute thickened vessels are included.

FIG. 99.

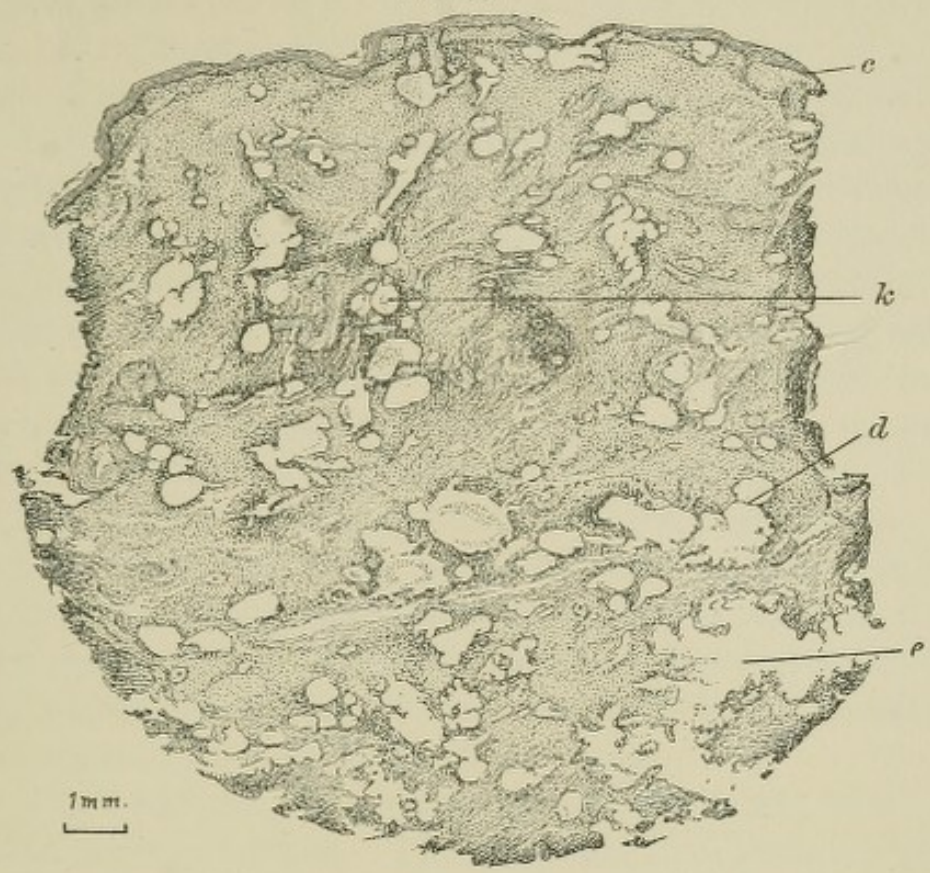
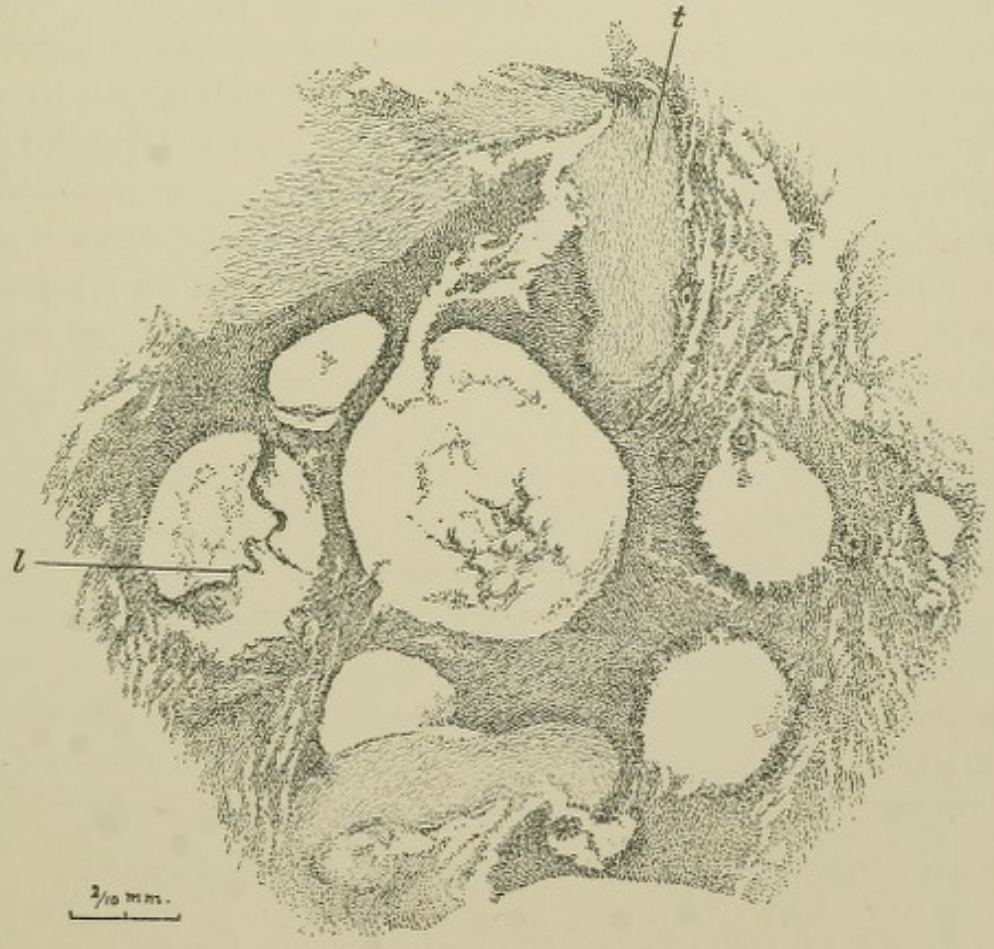


FIG. 100.



that have fibrous walls, while the larger ones lie directly in the splenic pulp. It is notable that cysts were found in four of the greatest organs of the same body, and it is probable that they had the same cause and the same mode of origin in all four. It is much the custom in medicine at the present time to attribute disease to infection, especially diseases which are obscure and difficult to understand, and when similar lesions occur in many different organs to attribute them to metastasis, which is but another way of expressing an extension of disease by infection from one organ to another. In this case of cystic degeneration certainly no process of infection was at work, but a common cause or tendency produced a similar effect in different and unrelated parts. The occurrence of cystic disease of four great organs is just as remarkable as that of cancer of several organs which is so common, and I have never been able to see that there is any greater reason for the assumption of the existence of an infective cause for the metastasis of cancer than there would be for a similar assumption in regard to the causation of the cysts.

Figs. 101 and 102 show a condition of the spleen which in my experience is very common. The section is from the spleen of a youth of seventeen who died of hypertrophy of the heart. Much of the tissue represented is natural, except that there is slight increase of fibrous tissue and the blood-vessels are very much thickened from obliterative arteritis, but part of it is full of minute holes. The contrast of appearance between that portion which contains the holes and the solid part is best seen in the low-power drawing, while the details of structure can be distinguished only in the one drawn with greater amplification. Cavities such as these have been described as pulp-sinuses,* and the condition named active hyperæmia of the spleen, but the cavities are represented as being filled with blood, while in my illustration it is seen that there is nothing like blood in any of them. Even if the cavities were filled with blood it would not prove that they were natural blood-spaces, for it has already been shown in connection with the liver (page 104) that in cases of congestion all the cavities and even the solid tissues become filled with red corpuscles, the blood forcing its way out of its natural channels and filling places in which it does not properly belong. Some of these cavities are more than one-half of a millimetre across, and they do not resemble any other known vascular space. The cells with which their lining is studded are more like those seen in cyst-walls than

* Practical Pathology, third edition, by G. Sims Woodhead, p. 417.

anything else. Such cavities are certainly not natural in the spleen, and to call them pulp-sinuses and suppose them to be blood-channels is an unsatisfactory way of explaining their existence. To assume that they are an early stage of cyst development would be premature, and yet the thought that such may be the case cannot be escaped. The case from which the illustration was taken was a youth who died of chronic disease, and chronic disease always makes those who suffer with it old before their time. In my experience, one of the commonest appearances in the spleen of old persons and of those who have died of chronic disease is the presence of such cavities as have been shown, and I believe it to be a disease which is not satisfactorily explained as acute hyperæmia of the spleen. Study of the spleen is to a certain extent unsatisfactory, as its function is unknown. So far as can be at present understood, it is seldom the site of primary disease, but, on the other hand, the morbid changes which occur in it are worthy of careful study, for no organ is more liable to change with the advance of years, and it always bears its part in the extensive diffuse lesions which accompany chronic disease, being especially liable to fibrosis, disease of its vessels and capsule, and adhesion to surrounding parts.

FIG. 101.—SMALL CAVITIES IN THE SPLEEN. (× 50.)

From a youth of seventeen years who died of hypertrophy of the heart with pericardial adhesion. *o* indicates the cavities, which are of varying sizes and shapes. The portion of spleen containing the cavities shades off into tissue which is natural in appearance, except that the vessels are thickened. The area *o* is represented more highly magnified in Fig. 102.

FIG. 102.—SMALL CAVITIES IN THE SPLEEN. (× 220.)

An enlarged view of the area *o* in Fig. 101. The cavities are lined with cells which it is difficult to classify. They are too large to be leucocytes, and have not their appearances, and yet they cannot be called epithelial cells.

FIG. 101.

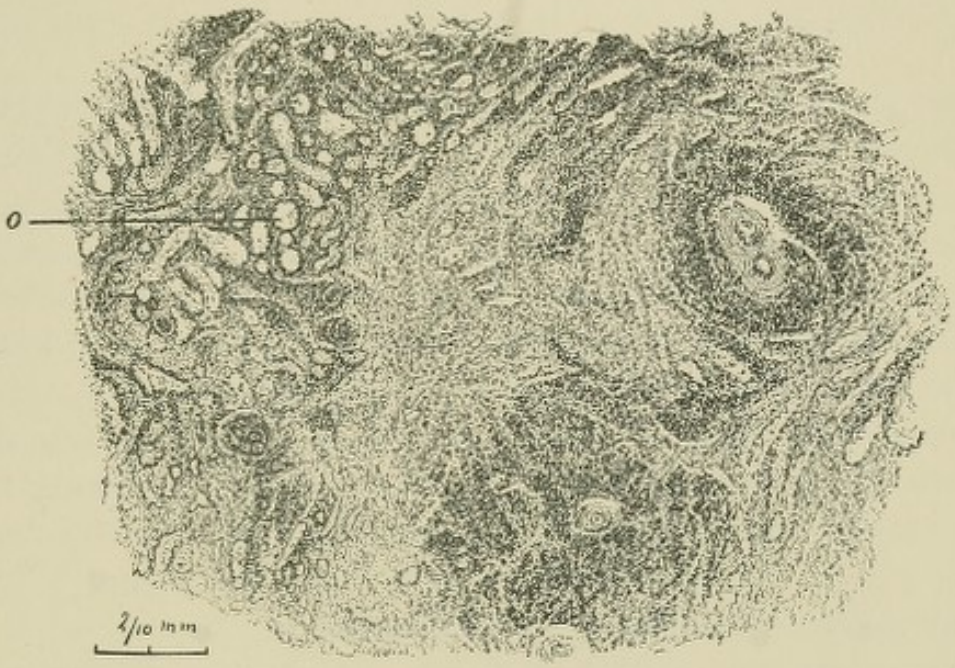
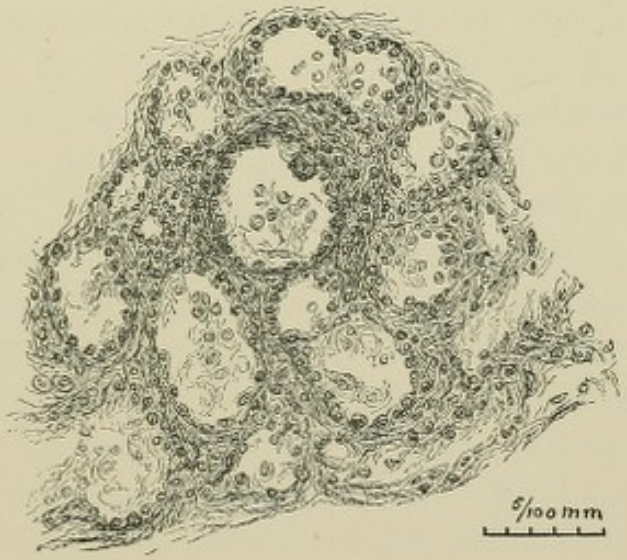


FIG. 102.



CHAPTER IX.

THE STOMACH.

THE stomach is an unsatisfactory organ in which to study minute pathological changes. When the lesions are gross, as is sometimes the case in cancer or ulcer, they are easily recognized, but even ulceration of the stomach is not always easy to understand, for it is impossible sometimes to know how much of the destruction which is seen was effected post mortem. A gastric ulcer itself may rapidly change after death. This difficulty of the study of disease of the stomach is true both of investigations made directly and of those with the microscope. The microscopical appearances of sections of human stomach taken from persons who have died of disease are so different from what we are taught by histologists is natural, that it is one of the greatest difficulties of the pathologist to decide to what extent the changes which he sees are the result of disease, or if they occurred post mortem. The histologist takes one of the lower animals, and, after killing it by some very rapid method, removes the stomach and places it in a preservative fluid before there is time for post-mortem changes to occur. It is curious that of all the human stomachs I have ever examined not one was lined with columnar epithelium, as we are taught is normal. The columnar cells are still found in the follicles, but from the lining surface they have disappeared. The rapidity of the post-mortem changes is attributed to direct maceration and destruction by the gastric juice. An almost exact parallel to this is found in the pancreas. Sections of human pancreas bear little resemblance to the normal, the characteristics of which have been learned from the tissue of lower animals. The cells are in such a condition that they cannot be satisfactorily studied, and this makes the preceding statement in regard to the stomach true also of the pancreas,—that study of its minute pathological conditions does not yield satisfactory results. Although the preservation of the cells in perfect condition is impossible, on the other hand there can be no doubt that consistent microscopical study of the stomach and pancreas and of the intestines carried out in all sorts of cases, whether or not there was any disease that could be recognized by the naked eye,

would yield very valuable results. In this way it would be possible for an individual investigator to acquire a personal experience of the appearances of the stomach which would enable him to recognize slight pathological lesions, instead of those only which are gross and therefore very obvious. A difficulty which always confronts the pathological histologist is to decide in the human tissues subjected to his examination how closely he may demand of them an approximation in appearance to accepted histological standards. An interval always elapses after death before an examination of a human body can be made, and in persons who have died of diseases like typhoid fever, in which the temperature is high, the tissues are softened and unsatisfactory to study so far as concerns the cells. It is almost certain that this soft condition of the tissues and the ill-defined state of the cells existed during life in such diseases, and are not purely post-mortem changes. During the course of diseases of this class, and especially during the later stages, when death approaches, the condition of relaxation is extreme, the tissues tending to slough, as is shown by the frequency of bed-sores. It does not seem, therefore, unreasonable to believe that the tissues have degenerated and the cells have lost their activity before death. It is as though the body had begun to decay before death occurred.

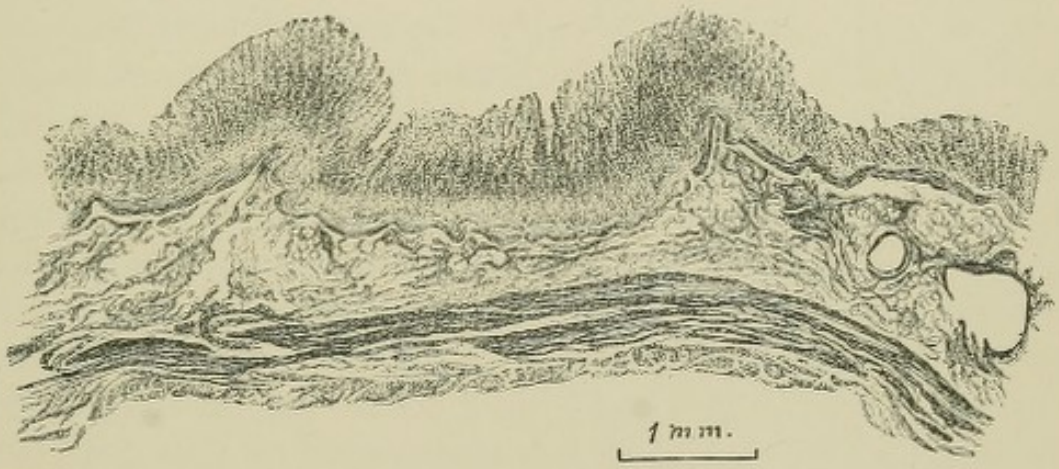
It is unusual to find a layer of pavement cells upon the capsules of the abdominal organs, or upon the surfaces of the lungs, or upon the lining of the pleural cavities. The capsules are usually simply fibrous membranes without any trace of a differentiated pavement layer upon the surface. The endothelial layer of the pleura and of the peritoneum which is so minutely described by histologists has almost no existence in human pathology. In consequence of disease or of post-mortem change, no trace of it is found. In old persons and in those who have suffered with chronic disease it is so usual to find the capsules of the abdominal organs and the pleural covering of the lungs thickened that one is tempted to think the endothelial layer disappears as life goes on and the coverings of organs become fibrous and thick.

The stomach calls for more frequent study, and such study will yield useful information. Fig. 103 represents a section of the stomach of a woman of thirty who died of Bright's disease after persistent vomiting lasting several weeks. The case has already been mentioned and illustrations given of the appearances of several organs,—heart muscular fibres, minute aortic aneurisms, and liver (Figs. 30, 31, 32,

FIG. 103.—DEGENERATION OF THE STOMACH. (× 13.)

From a woman aged thirty years who died of Bright's disease, having had persistent vomiting for many weeks. The mucous coat is not normal; it is of uneven thickness, and the follicles cannot be recognized, to such an extent have they melted together. Epithelial cells are not distinguishable. The submucous coat is a little thick and loose-meshed, but neither it nor the muscular coat presents any definite appearances of disease.

FIG. 103



53, and 87). The appearance of the stomach is unusual, and has been produced by disease. The follicles and cells have lost their distinctness, having run together to form a layer which is thicker than the natural mucous coat and is much more nearly homogeneous. The disease is confined to the mucous layer. It does not seem surprising that a person with the lining of the stomach in such a condition should have vomited and been unable to assimilate, for there remains hardly one of the mucous cells which play so important a part in digestion. The vomiting was so obstinate that it was impossible to decide during life if the disease was cancer. The microscopical examination answered this with an absolute negative. In another case of continued vomiting combined with the symptoms of meningitis the whole pyloric end of the stomach was found to be four or five times thicker than natural. The thick portion was of soft consistence and symmetrical around the pyloric ring, instead of being greater on one side than on the other, as is usually the case with cancer, which generally begins at a single centre and thence extends. There was great thickening of the submucous and muscular coats, but no cells or combinations of cells characteristic of cancer could be found. It is sometimes easy to recognize cancer from the gross appearance of the specimen, or, again, a section examined with the microscope will furnish the proof. In such a case as the one described, the indications being indefinite, it is an easy escape from a difficulty to say the disease was cancer; but such an assumption is neither scientific nor conclusive. There were symptoms of meningitis during life, and after death was found advanced disease of the peripheral nerves within the spinal canal, although none of the cord itself. The result, therefore, after clinical study, post-mortem, and microscopical examination, was uncertainty as to the cause of death. There are few things more puzzling than such cases as the two described, the first a woman with lesions in several organs, these being of old age or fibroid nature, and the second a man with unrelated states of disease of the nervous system and stomach. There must be an underlying cause, which as yet remains undiscovered, to produce such strange results.

CHAPTER X.

THE INTESTINES.

WHAT has been said of the stomach is true also of the intestines,—that consistent study of their gross and microscopical appearances in diseases not known to produce lesions in them would yield most useful information. Examination of the intestines is more satisfactory than that of the stomach, for they undergo less rapid post-mortem change. Figs. 104 and 105 represent an ulcer of the colon of a woman twenty-six years old who died of typhoid fever. They demonstrate several points of interest: first, ulceration in typhoid fever does not usually involve the colon, but is confined to the ileum; second, there are cavities in the thickened submucous coat; and, third, there is amyloid disease of the submucosa. With regard to the first, ulceration of the colon in typhoid fever, it is interesting, but not extraordinary, for in any great number of cases of the disease ulcers will sometimes be found in the large as well as in the small intestine. The cavities in the tissue might possibly be taken to be the result of fatty degeneration of the thickened submucous layer, but an examination of the second drawing, made with greater amplification, shows that this was not the case. They lie in the midst of inflammatory tissue and adjacent to the region of amyloid deposit, and when thus seen considerably magnified it is evident from the nature of their walls that they are not fat cells. One is driven back, therefore, to the statement already made in the discussion of the cavities which are so common in the liver (page 104), that they cannot be explained as the result of fatty degeneration, and that to call them vacuoles is only to give a name to what is not explained. There is strong reason to suppose the cavities are the effect of a process akin to cystic degeneration, if they are not simply cysts of small size. Whether fatty degeneration has any connection with this disease cannot be now ascertained. In the liver it was shown that cavities of all sizes, from those which are evidently the result of fatty degeneration to cysts large enough to be seen with the naked eye, may be found in the same liver, and it was stated also that in the case of the smaller-sized ones it is impossible to distinguish precisely between fat cells and small cysts. The amy-

FIG. 104.—ULCER OF THE COLON SHOWING AMYLOID DEPOSIT. (× 11.)

From a woman of twenty-six years who died of typhoid fever. *b* is placed over the ulcer. *x*, *y*, and *z* are the mucous, submucous, and muscular coats. The mucous coat is interrupted, and the submucosa much thickened and infiltrated at the ulcer. At *c*, in the submucosa, are many holes, and to their right and below them is the amyloid deposit. The holes are such as are commonly described as due to fatty degeneration, or as vacuoles. *c*, with the surrounding region, is represented more highly magnified by Fig. 105. This drawing shows the relative situation of the parts, but the greater amplification of Fig. 105 is necessary for the exhibition of the nature of the structural changes.

FIG. 105.—ULCER OF THE COLON SHOWING AMYLOID DEPOSIT. (× 50.)

Enlarged view of the region *c* of Fig. 104. *c* indicates the holes, and below and to their right is the amyloid deposit (*s*). The deposit is in whorls or appears longitudinally striated as it happened to be cut, and is infiltrated with cells, as is usual in amyloid material. At the centre of the ulcer (*r*) is a fissure, and upon either side of it are areas of round-cell infiltration. This amplification demonstrates that the holes are not fatty deposit. Fig. 126, which represents typical amyloid disease of the kidney, should be examined with this illustration, and it will be seen how precisely alike the two are.

FIG. 104.

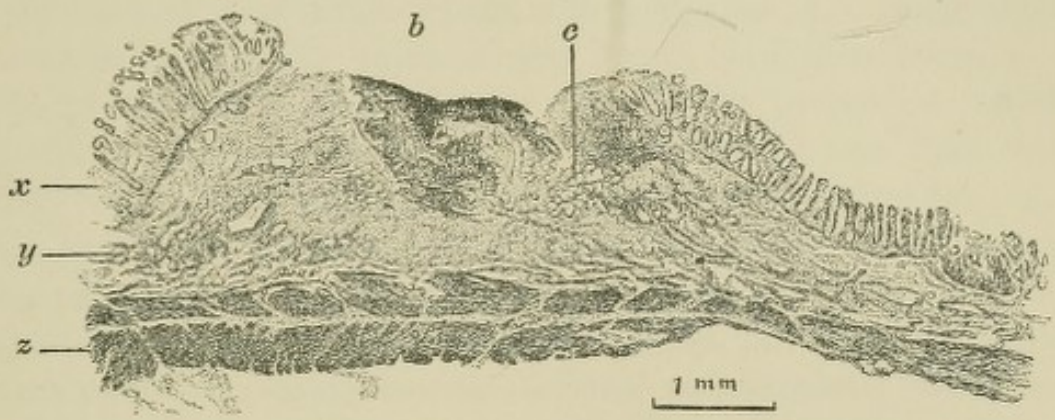
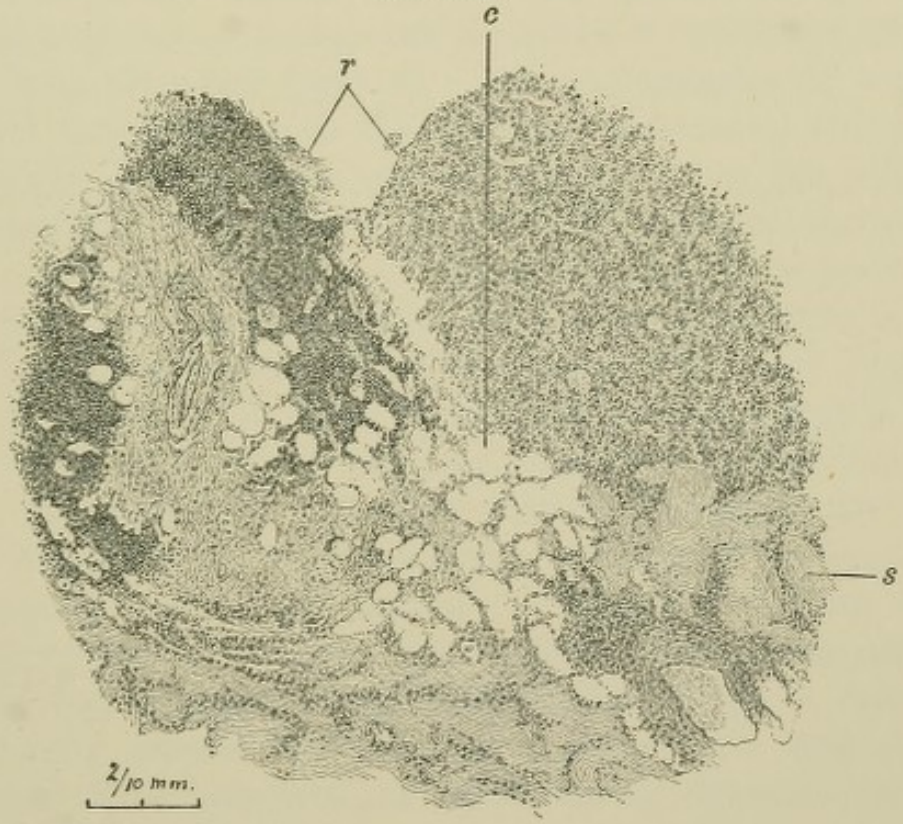


FIG. 105.



loid disease (Figs. 104 and 105) is not of great extent, but is very distinct. In such a case, in which the amount of amyloid deposit is small, its relation to the tissue with which it is surrounded can be easily studied, and the impression that the whole process is only a form of fibrosis becomes very strong. The amyloid deposit has the homogeneous and glassy look which is characteristic of it, and through it extend lines of connective tissue containing nuclei. Such amyloid material is exactly like some of the forms of fibrous tissue. The difference is that in most fibrous tissues the proportion which is nucleated is greater and the structureless material less than is seen in Fig. 105. The tissue was not subjected to the iodine test, for the reason that when the post-mortem examination was made there was no suspicion of the existence of amyloid disease. The case affords another exemplification of the fact already so frequently dwelt upon, that in cases of disease having definite pathological lesions other lesions quite foreign to those accepted as properly belonging to it will often be found if sought.

The intestines when healthy are very thin, but they sometimes become excessively loaded with fat. The question of the extent to which the organs may accumulate fat before it constitutes disease has already been discussed (page 8). The accumulation of a moderate amount of fatty tissue upon the intestines in stout or elderly people is not to be looked upon as unhealthy, but, on the other hand, when there is a thick layer of fat upon their exterior and masses of it hang upon them, as is not infrequently seen, they must at least be sluggish in the performance of their functions, if there is no more injurious effect induced. In elderly people who have died of dysentery the colon is so often found thick and fatty that it is likely this is more than coincidence, nor is it rare to find that persons dead of dysentery had had other chronic disease, as, for example, Bright's disease or chronic bronchitis. It must not be forgotten that the dysentery seen in this latitude is generally different from the dysentery of tropical countries, which often attacks young persons and those who had been previously in perfect health and is rapidly fatal. In an elderly woman who died of dysentery and Bright's disease and whose heart presented an extraordinary development of fatty infiltration (see Figs. 46 and 47) the colon was in a corresponding fatty condition. When examined in section it looked like a piece of adipose tissue, and could not have been recognized as colon by its appearance alone. The ulceration had entirely removed the mucous

follicles, the submucous and muscular coats were infiltrated with fat so as to be beyond recognition, and outside of them was a layer of fat which was thicker than the gut itself. This state of disease resembled in many respects the fatty infiltration of the heart which was found. In both heart and colon the layer of fat upon the outside was thicker than the organs themselves, and the tissue was distorted and split apart by fat-infiltration. It is impossible not to believe that the deposit and infiltration of fat must have been very destructive of the power of the organs to perform their functions. It is probable that the dysentery which was the direct cause of death was induced by the fatty infiltration, for tissues in process of infiltration with fat are thrown into a condition of exaltation which renders them liable to inflammation. A parallel can be drawn to a certain extent between very fat people and fatty organs. The very fat are, as a rule, puffy and incapable of as much labor as those who are better proportioned. Their power of sustained effort is reduced, and they are liable to succumb to acute attacks so slight that they could have been easily borne by persons of normal resisting power. The fat deposited in and upon the colon varies in character in different cases. Sometimes it has the delicate and finely reticulated appearance which is characteristic of normal fat, and again it may be of much more dense consistence and have bands of fibrous material running through it. When the latter is the case it must be considered that the condition is partly fibroid disease. It will presently be shown that this combination of fibroid disease and adipose deposit occurs in the perirenal fat, and it has already been discussed in connection with the fat layer upon the heart. The presence of small amounts of amyloid deposit in the intestines, or at any rate of material which is so like it that it cannot be said not to be amyloid, is very common. For instance, an illustration has already been given of an arteriole (Fig. 16) in the colon of a man who died of dysentery induced by acute lead poisoning. The gut was enormously thickened, the stage of ulceration not having been reached, and some parts of the thick mucous coat looked amyloid.

The study of the pathological conditions of the intestines which I have been able to make has not been without profit, although less satisfactory, because less extensive, than that of the heart, lungs, liver, spleen, and kidneys. The existence of minute cavities, probably the result of cystic degeneration, in an ulcerating colon indicates the likelihood that cystic disease is a common and very generalized process, for

it has already been shown that cysts are common in the liver and spleen. If it could be shown that amyloid disease is only a form of morbid fibrosis, another link would be formed in the chain to connect diseases which have been looked upon as widely separated, but which really are nearly related. It has been taken for granted that disease ordinarily has a single point of origin, when in truth it often arises simultaneously in several places, owing its origin to causes as yet beyond our comprehension.

CHAPTER XI.

THE KIDNEY.

THE pathology of the kidney has been more thoroughly and profitably studied than that of any other organ, and its anatomy, to the minutest details, is better understood. Its function is one of the most important in the economy, and a parallel may be drawn between the importance of the excretion of fluid from the body and the urgent necessity for its frequent imbibition. Persons soon die of thirst if the supply of liquid is cut off, but starvation is a slow process. After the brain, heart, and lung, the next organ in importance is the kidney, and its entire cessation to act causes death more rapidly than anything except the failure of one of the three organs first named. The kidney is prone to disease, and it changes with the progress of years as surely as wrinkles come in the faces of the aged. On the other hand, it is wonderful how tolerant it is of injury. Nature has made such bountiful provision of renal tissue that a great part of it can be diseased and yet a condition of tolerable health be maintained. It is well known that one of the kidneys may be entirely destroyed and the remaining one still suffice for the maintenance of life. The kidney in early infancy is different in appearance and occupies a different position from the appearance it presents and the position it occupies in adults. In young infants the capsule is thin, delicate, and entirely transparent, and the organ seems to stand out uncovered in the abdominal cavity, although from the anatomical stand-point it is post-peritoneal and not in the abdominal cavity. The fat with which it is later surrounded is entirely wanting. In infancy the greater free curvature of the kidney projects much more toward the front than it does in adult life, when the organs are flat against the back of the body, the hilum of each toward the spine, and the greater curvatures toward the two sides. The minute anatomy of the kidney is different in infants. In preparations made for microscopical examination, if the plane of section is vertical to the surface, the tubules and vessels are cut in their length, in which case the relation of the Malpighian bodies to the tubules is displayed. In such instances in infants it can often be seen that the Malpighian bodies are arranged around the tubules so as

to produce the effect of a tree with fruit hanging from its branches. There is a central stem of tubules with the rounded Malpighian bodies disposed upon each side. This disposition of the various parts is well known to histologists, and pictures illustrating it are included in many works upon that subject. In infants' kidneys it is very common, perhaps usual, to see this anatomical arrangement more or less well displayed, but in adult kidneys, of which I have examined ten times more than of infants, I have never seen it. This experience, although not so extensive as might be desired, is sufficient to prove the point, that the minute anatomy of the kidney changes as life goes on; that at later periods confusion takes the place of the beautiful and simple order which existed when the period of most active development closed. As a result of disease this loss of orderly arrangement may be pushed to its extreme limits. In the natural kidney large blood-vessels exist only at the junction of the cortical and medullary portions, where they enter the organ, for soon after leaving this region they break into small twigs, so that the subcapsular tissue contains no large arterioles and but few Malpighian bodies, which are numerous a little deeper in the organ. It will be presently shown that in contracted kidneys large-sized blood-vessels are often found close to the external surface beneath the capsule, and great numbers of Malpighian bodies crowded nearer one another than is natural in the same region. This extreme distortion must be the result of the growth of the morbid fibroid tissue, which pushes the blood-vessels and Malpighian bodies toward the surface and destroys entirely the natural arrangement. It is very common to find cysts in the kidneys of old people, so that by many it has been considered natural; but such a conclusion is surely erroneous, for the formation of cysts in the kidneys is a destructive process as much as is the formation of cavities in the lungs, and the one cannot be natural any more than the other. No one would look upon cavities in the lungs as a natural result of old age. To distinguish between the changes natural to the advance of years and those of disease is a difficulty ever present to the pathologist, but in the case of cystic kidneys it is easy to decide to which class they belong. A singular antithesis to this, and at the same time a confirmation of its truth, is the fact that the kidney, like all the other organs, is subject even in early infancy to changes which at later periods are attributed alternately to age and to disease. At six weeks I have seen large thrombi in the renal veins and casts in the secreting tubules. At five and six months marasmic babies—and

such infants always resemble octogenarians—will often be found to have the capsules of the kidneys of irregular thickness, the fibrous tissue increased, and the tubules dilated, just as they ordinarily are in Bright's disease. In one of my cases, an infant of six months, there were found several calcareous deposits in the kidney and a stone which, after drying, weighed about one and one-fifth grains and was a quarter of an inch across in its longest diameter. The infant was a foundling that had been neglected, and it was shrivelled and wrinkled so that it appeared a veritable type of age. This deposit of calcareous matter, with the aged appearance of the infant, indicates that tissue-changes usually considered as natural to age and those of chronic disease are more nearly related than at a superficial view would appear. Since the lesions of disease of such a character are to be found in infancy, it is not surprising that they exist also in childhood and at all later periods of life.

Fig. 106 represents a portion of the kidney of a girl of ten years who died of heart disease and who had amyloid degeneration of the liver, spleen, and kidneys. There is thickening of the capsule, and the thick portion is sunk into the renal tissue, making a depression beneath which the tissue is diseased. The Malpighian bodies remain, but do not appear healthy, the capillary loops being shrunk and surrounded by a greater amount of open space than is natural. The secreting tubules have almost entirely disappeared from the diseased region, which is in an early stage of fibrosis. In this instance also the thickened portion of the capsule is of open structure and contains many nuclei, whereas in older people and when the disease is advanced the fibrous and thick capsule is generally very solid and contains but few nuclei. The disease as represented by the drawing is typical of the beginning of fibrosis and contraction of the kidney, although the tissue is less solid than is usual in older persons and at more advanced stages. Fig. 107, which is from the same kidney as the foregoing, shows an arteriole passing into the kidney from the perirenal fat through the capsule. It is an anatomical fact not so generally known as it might be that, besides the renal artery which enters at the hilum, the kidney receives minute arterial branches from various sources which pass directly through the capsule to enter the substance of the organ. When the mode of development of the kidney during the embryological period is remembered, it seems as if there must have been a time when no vessels entered it through the capsule; but, however this may be, my experience has led me to believe that

FIG. 106.—EARLIEST STAGE OF CONTRACTED KIDNEY. (× 50.)

From a child ten years old that died of heart disease. *c* and *h* indicate the boundaries of a fibroid area; in it the tubules have almost disappeared, but the Malpighian bodies persist. In the tubules to right and left of the fibroid region the epithelial cells are ill defined. The capsule is thickened and shredded out, and over the fibroid area it is thickest and dips downward. This thickening of the capsule with a dip below the general level of the surface of the kidney and an area of fibrosis under the depression is characteristic of the beginning of contraction.

FIG. 107.—ARTERIOLE ENTERING THE KIDNEY FROM THE CAPSULE. (× 50.)

Another area from the same section as Fig. 106. *v* indicates the arteriole which is entering the substance of the kidney from the perirenal fat. At the point of entrance the renal tissue is unnaturally fibroid.

FIG. 106.

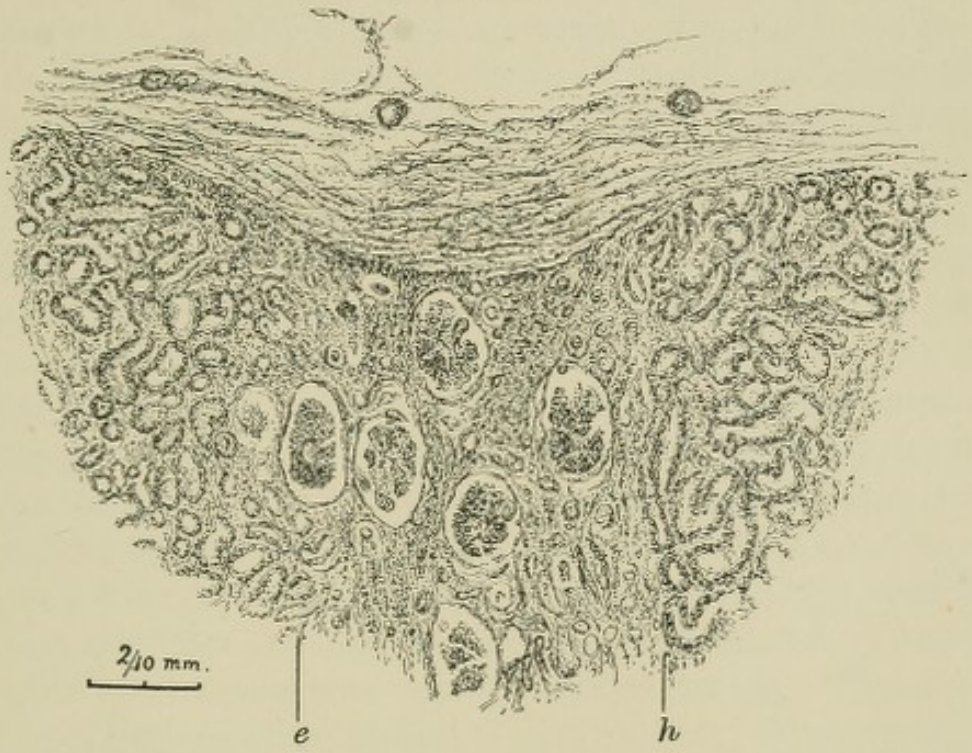
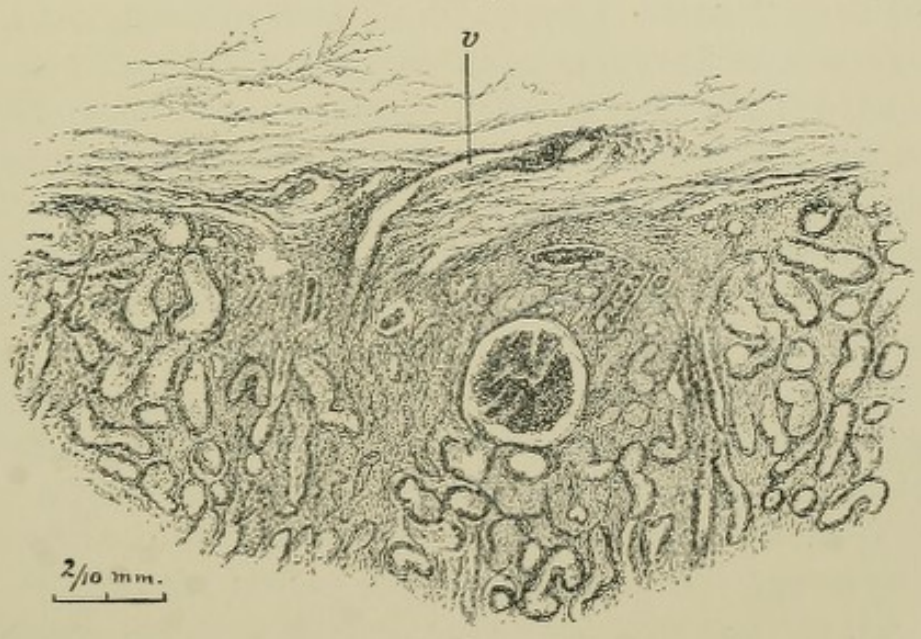


FIG. 107.



these capsular vessels are greatly influenced by disease. It is probable that in fibroid kidneys they increase in size and prominence and in numbers. In healthy kidneys the vessels that penetrate the capsule are not noticeable in making the ordinary manipulations of a post-mortem examination, so minute are they, but in contracted kidneys if the capsule is pulled off they are seen to be numerous and to appear like stout cords binding the capsule to the kidney. The drawing shows that at the point of entrance of the vessel there is disease of the kidney of a character similar to that which has been described in connection with the preceding illustration. There is a slight pit of the surface of the kidney at the point of entrance, and the capsule is thick and the tissue in the immediate neighborhood has been condensed by fibrosis, so that in part of it the tubules have nearly disappeared, while around the fibrous area they are much dilated. In several other instances I have examined portions of diseased kidneys containing one of these arterioles passing through the capsule, and in every one of them the point of entrance was the seat of fibrosis. This conjunction of fibrosis with vascular disease is very curious. It was first described by Gull and Sutton in their essays upon arterio-capillary fibrosis which now belong to the classics of medicine. The origin of the process is still unknown, it being impossible to decide whether it begins in the arteries or in the fibrous tissue around them or in both. The child from whose kidney the two foregoing illustrations were taken was, as has been said, ten years old, and it has been made very evident that there was fibroid disease. The case illustrated an interesting fact in connection with amyloid degeneration. The liver, spleen, and kidneys showed the peculiar reaction of amyloid material when tested with iodine, and the liver and spleen when examined microscopically were seen to contain great quantities of the deposit. In the kidneys, however, the evidence of amyloid disease as determined by the microscope was so slight that if it had not been that the liver and spleen were so very amyloid, and that the kidneys had reacted to the iodine test, it would have been impossible to determine that they were so diseased. The only amyloid deposit visible in the kidneys was in the Malpighian loops, in which there were a few of the peculiar homogeneous spots. The kidneys therefore showed minute pittings of the surface with fibroid tissue beneath, and the capsule was thickened; these are the most positive signs of contraction of an early stage; but besides all this there were minute patches of homogeneous deposit in the Malpighian loops which were certainly amyloid, for the tissue had

shown the peculiar reaction with iodine, and the liver and spleen were in the last stages of amyloid degeneration. Homogeneous spots in the Malpighian loops, as described, are in my experience exceedingly common in chronically diseased kidneys, and many times in cases in which they were present, but in which there was no other reason to suspect the existence of amyloid disease, I have been unable to determine whether or not there was amyloid change. There can be no distinct line drawn separating fibrosis from amyloid degeneration, and, as has been said in connection with the intestines and some of the other organs, there are many reasons for believing them to be only variations of the same disease. At nine, twelve, fourteen, and seventeen years, just as in the case of the girl of ten, I have found in the kidneys areas of fibrosis, thickening of the capsule, some tubules greatly dilated and others very small, casts in the tubules, and all the other signs of Bright's disease. In children, therefore, the lesions of chronic disease of the kidney are similar to those common in older persons and in old age, and even in infants of a few months the parallel holds good, for it has been shown that stone in the kidney, which is usually a disease of advanced life, may exist in an infant of six months with marasmus.

Fig. 108 represents a minute fibroid spot in the kidney of a man of twenty-seven who died of acute cholera morbus after an illness of less than forty-eight hours. The existence of a morbid fibroid spot under the circumstances is again illustrative of the fact so often mentioned that lesions of chronic nature other than those belonging to the disease which caused death are often found if sought. It suggests again the important question, To what extent is the outcome of attacks of acute disease influenced by the degree of bodily perfection of the individual when attacked, and how much more liable is a person with lesions of latent disease to have acute attacks than one whose condition is more nearly perfect?

The commonest disease of the kidneys is fibrosis, or, as it was formerly more often called, contraction. Since the time of Bright the pathological condition has probably been more extensively investigated than any other disease to which man is subject. It produces a great variety of different appearances, both gross and microscopical, due to the manner in which the tissue is affected and the extent to which the disease has progressed.

Figs. 106 to 115 represent types of fibroid kidney, but they are very different, owing to the varying ways in which the tissue has

FIG. 108.—SMALL FIBROID SPOT IN THE KIDNEY. (× 105.)

From a man twenty-seven years old who died of acute cholera morbus. *a* is the fibroid area, which is composed of connective-tissue cells and fibrous strands running in many directions.

FIG. 109.—FIBROID KIDNEY. (× 15.)

From a man fifty-seven years of age who died of Bright's disease. The capsule is greatly thickened, but especially so at the middle part of the picture, where it is depressed below the general level, and underneath it the kidney is fibroid. The tubules and epithelium have here disappeared, and their place is taken by fibrous tissue and the round cells of inflammatory tissue. This fibro-inflammatory material is most dense and in greatest mass directly beneath the thickest and depressed portion of the capsule, and from this it branches out in various directions. The tubules which occupy the space between the fibroid lines and patches are almost all dilated so as to be much larger than natural. Malpighian bodies in various stages of destruction are scattered through the tissue.

FIG. 108.

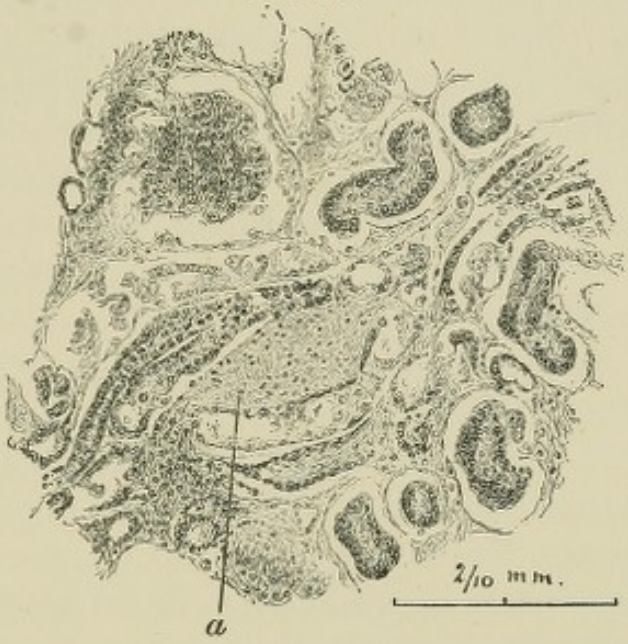
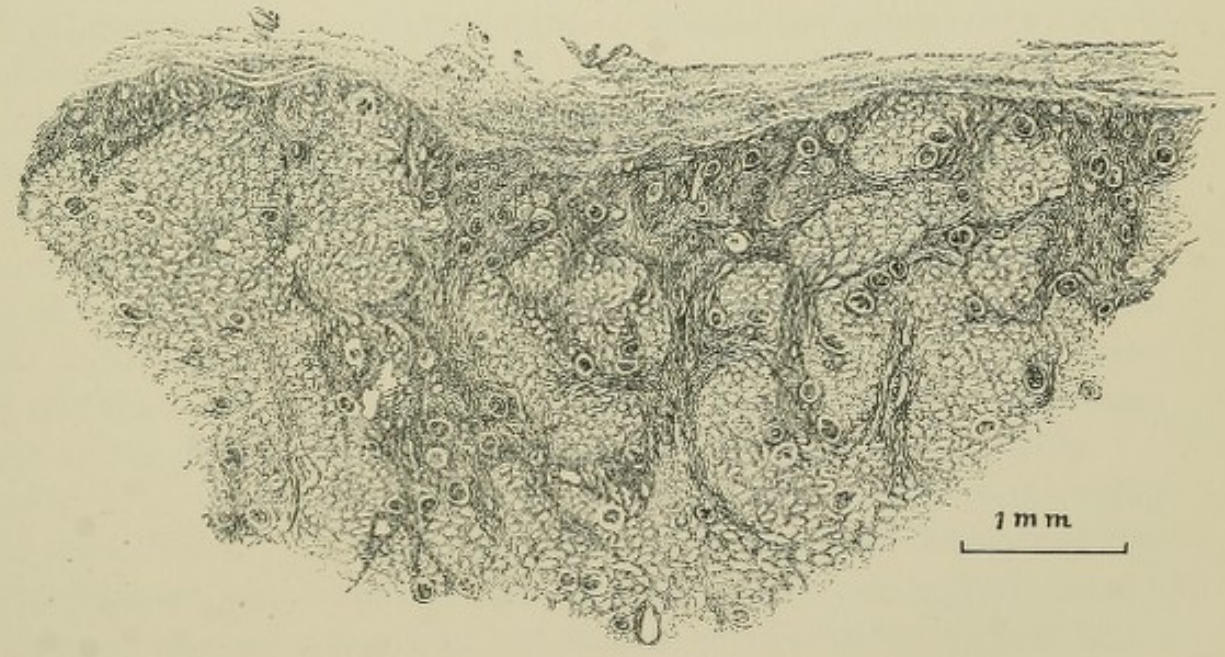


FIG. 109.



been destroyed. It is not easy to be certain which manner of destruction is the most common, but probably it is that represented by Fig. 109, which is from the kidney of a man of fifty-seven who died of Bright's disease with extensive fibrosis of most of the organs and deposits of chalk in a great many different tissues. The capsule is greatly thickened, and where thickest is sunk into the kidney tissue, making a depression below the general surface level. Beneath this depression is a fibroid area which examination under greater amplification would show to be composed of round-cell infiltration and fibrous strands, interspersed with Malpighian bodies in various stages of fibroid destruction. Epithelium and all appearance of tubules have almost entirely disappeared from the fibroid areas. Scattered all through the tissue are fibrous strands similar to the large mass beneath the thickened and depressed portion of the capsule, and it appears as if these strands had grown by extension from the main fibroid mass. The remaining renal tissue is still composed of epithelium, but almost all the tubules are dilated so that they are very much larger than natural. It is striking how the disease seems to have its centre and to have originated at the external surface of the kidney in a region where the capsule is thickened and depressed and the tissue beneath fibroid. Such lesions look like a further development of what has already been illustrated by Fig. 106 as the earliest stage of contracted kidney. In this form of fibrosis the greatest portion of the tissue is natural, consisting of tubules lined with epithelium. The tubules, although very much dilated, were not so greatly injured but that they could perform their function and in case of the recovery of the patient might have again become natural. The clinical history of such cases usually is that the excretion of urine had been sufficiently good for the maintenance of life, and that the direct cause of death was to be sought elsewhere than in the kidney, probably in the lungs or the heart, although according to the accepted method of classification of the day the case was called Bright's disease of the kidney.

Fig. 110 represents a portion of kidney from a man fifty-one years old who died of perihepatic abscess. The diagnosis during life was typhoid fever, and, although the symptoms were not typical and the diagnosis was not considered satisfactory or conclusive, a more accurate one could not have been made. It was only at the post-mortem examination that a large perihepatic abscess was found to be present and no lesions of typhoid fever whatever. The drawing includes a portion of the kidney with the capsule and some perirenal fat. The

condition is different from that last described. Instead of the disease being scattered in spots, the whole of the tissue is diseased. The effect produced is that of a fine fibrous tissue with Malpighian bodies and epithelial tubules scattered through it. The amount of epithelium is insignificant and that of fibrous tissue enormous, and it has forced the tubules apart so that hardly any two are in contact as is natural. The tubules are all narrowed and some nearly closed, a condition very different from that shown in Fig. 109, in which the tubules are dilated. The Malpighian bodies are in all stages of fibroid destruction. The capsule is thick and of coarser texture than natural, and the fibrous strands composing it do not all run parallel with one another to produce a smooth outer surface, but many of the surface strands run off at right angles to the general line of the capsule. These right-angled fibrous bands run out into the perirenal fat and are sometimes continuous with fibrous tissue, of which there are strings running in various directions through the fat. This condition of fibrosis of the perirenal fat with thickening of the kidney capsule and close binding together of the capsule and fat is a very common accompaniment of contraction of the kidneys, and it has been shown that a parallel condition occurs in the heart and its fatty layer. A portion of the same section is represented more highly magnified by Fig. 111 (see description), which shows one Malpighian body very fibroid, others somewhat shrunken, the tubules undergoing atrophy, and that much the larger part of the kidney included in the drawing, instead of being almost entirely epithelium, as would be natural, is composed of fibrous tissue. Details of structure are better shown by this drawing, but the general effect of the universal growth of fibrous tissue, the thickening of the capsule, and the unnatural adhesion to it of the perirenal fat, which is also unnaturally fibrous, all characteristic features of the form of contraction, are seen at a glance in the low-power picture.

Fig. 112 illustrates a third form of fibrosis. It is a portion of the kidney of a man of fifty-eight who died of Bright's disease. This kidney is strikingly like inflamed emphysematous lung, which when examined under moderate amplification appears as a solid tissue with open spaces scattered through it, the solid portion being lung tissue of which the alveoli have been filled with exudate, and the open spaces dilated and broken air-sacs which have remained empty. The kidney is diseased so that it is almost beyond recognition. Only a small portion of the tissue included in the drawing is composed of the epithelial tubules, most of it being fibrous material which is rich

FIG. 110.—FIBROID KIDNEY. (× 16.)

From a man fifty-one years old who died of perihepatic abscess. This presents a strong contrast with Figs. 109 and 112. The disease is generalized instead of being in spots; everywhere there is a great increase of fibrous tissue, which is translucent and poor in cells, the Malpighian bodies are small, the tubules of small calibre, and the total amount of epithelial tissue reduced so greatly as to be insignificant. The capsule is thickened, and there extend from it fibrous strands which ramify in the perirenal fat. The area indicated by *u* is represented in Fig. 111 more highly magnified.

FIG. 111.—FIBROID KIDNEY. (× 50.)

The area *u* in Fig. 110, more highly magnified. This shows the nature of the fibrous tissue,—that it is poor in cells, and that the amount of epithelial tissue is diminished and its cells are disintegrated. *q* is a fibroid Malpighian body.

FIG. 110.

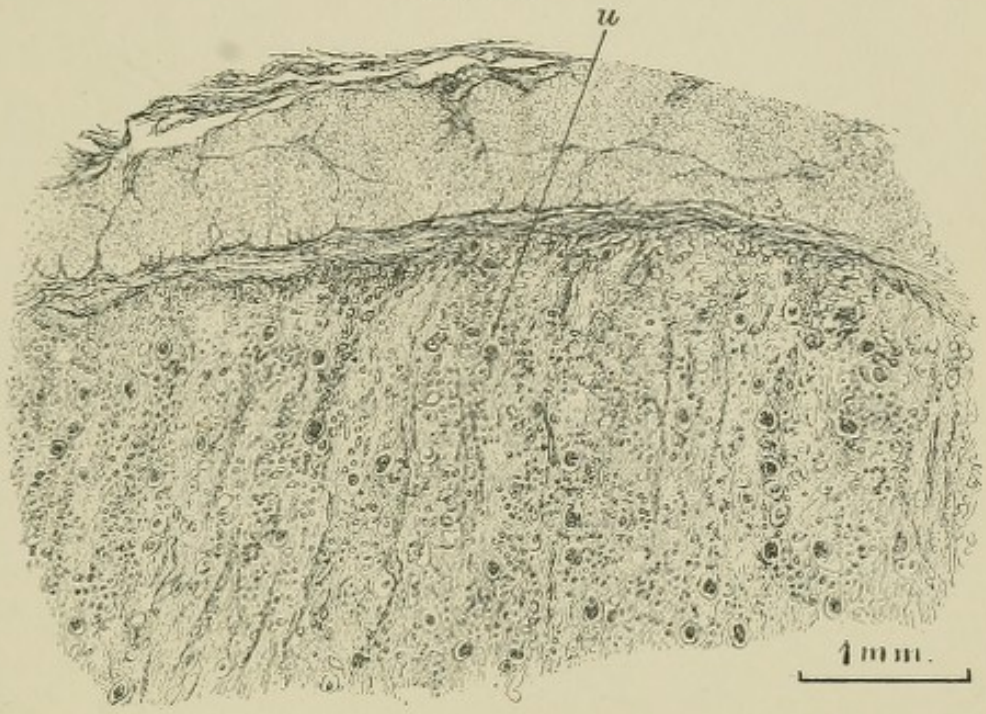


FIG. 111.

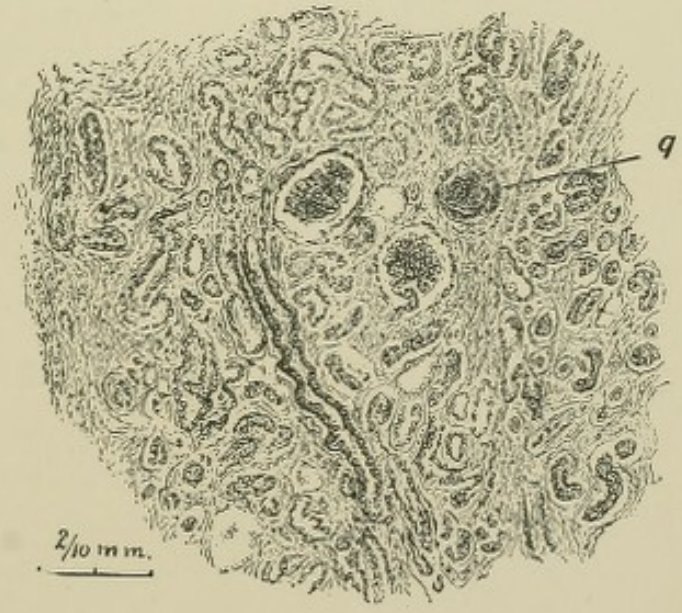


FIG. 112.—FIBROID KIDNEY (RESEMBLING PULMONARY EMPHYSEMA). (× 10.)

From a man of fifty-eight years who died of Bright's disease. The general appearance recalls that of pulmonary emphysema ; the patches containing dilated, broken tubules which are adjacent to the surface and project beyond the general level are like emphysematous blebs on the surface of lung ; there is great increase of fibrous tissue, which is very dense and rich in inflammation cells ; the epithelial elements which remain present themselves as islands in a sea of diseased fibrous tissue. These epithelial islands consist of dilated tubules and tubules with broken walls, like lung alveoli in emphysema. The contrast of this mode of destruction with that depicted in Figs. 109 and 110 is most striking. *g* is placed above the area represented more highly magnified in Fig. 113.

FIG. 113.—FIBROID KIDNEY (RESEMBLING PULMONARY EMPHYSEMA). (× 50.)

Enlarged view of the area *g* in Fig. 112. The capsule, which is greatly thickened, is raised over the central region which contains the dilated and broken tubules, and dips slightly over the fibroid areas to right and left. A Malpighian body is included in the central region. The great density of the fibrous tissue and its richness in the round cells of inflammation are well represented. In what respect does this process of destruction differ from that of emphysema of the lung?

FIG. 112.

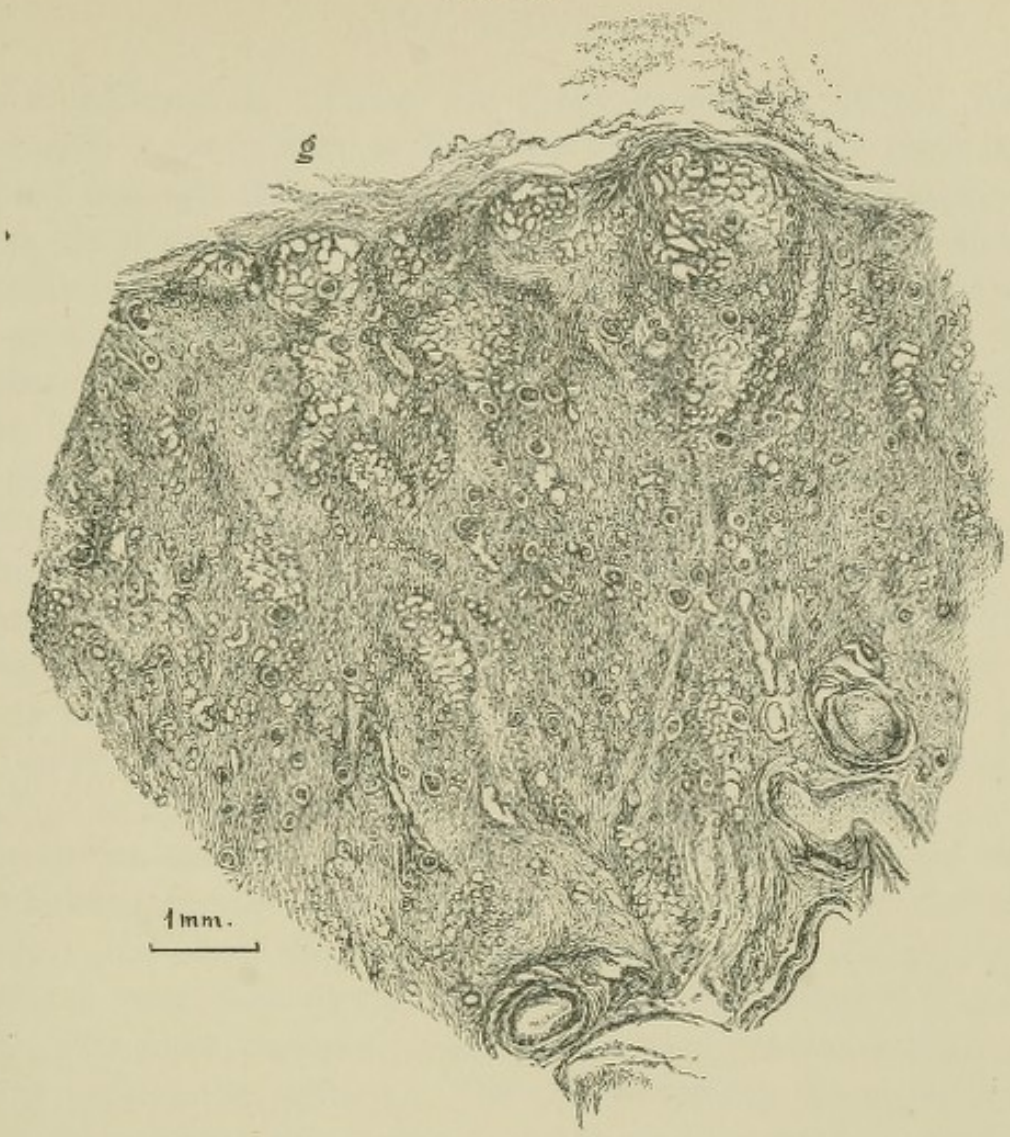
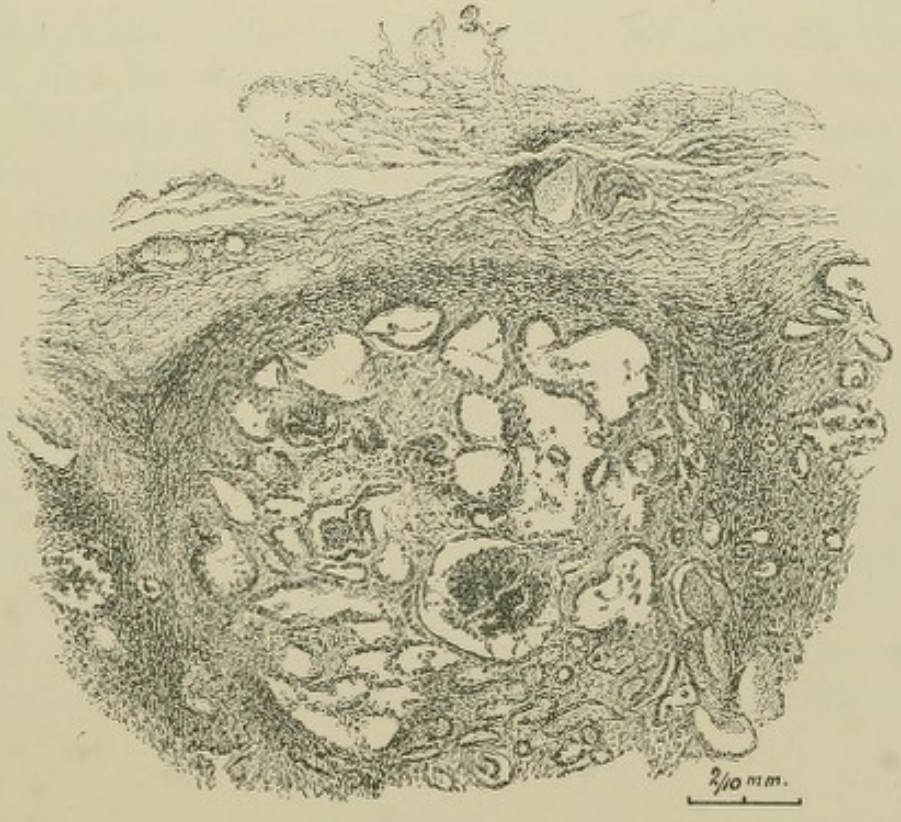


FIG. 113.



in inflammation-cells. There are areas containing dilated tubules whose walls have broken so that they form good-sized open spaces scattered through the general fibroid mass. Several of these open patches are at the surface, and in such instances they form projections so closely resembling emphysematous blebs upon the surface of the lung as to suggest a parallelism of the two states of disease. There is always fibrosis with emphysema of the lungs, and its most salient feature is the way in which the walls of the air-sacs break down to form large empty spaces exactly as has happened to these renal tubules. The drawing includes the entire depth of the kidney from the capsule to the hilum, and therefore shows all the parts. The differentiation of the medullary from the cortical substance, which in healthy kidney is very sharp, has been entirely destroyed by the disease, so that straight tubules, labyrinths, cortex, and medulla are all alike, except that the largest vessels are confined to the region of the hilum. The appearance of the kidney affords a most striking confirmation of the statement that disease often entirely destroys natural topographical arrangements. One of the large arteries is filled with a thrombus, and when the section is examined with sufficient amplification it is seen that all the arteries are greatly thickened and diseased. The most common condition of these arteries is thick walls, tending to close the calibres. The tissue forming the walls is much more homogeneous than natural and is poor in cells; therefore the differentiation of the coats is nearly lost. Such arterioles strongly resemble vessels which have undergone the amyloid change. Most of the Malpighian bodies are fibroid, they are generally reduced in size, and, like the walls of the arterioles, tend to be homogeneous. In some instances it is difficult to distinguish between arterioles and Malpighian bodies, to such a degree has the fibroid degeneration changed them, and yet few things are more unlike than healthy Malpighian bodies and arterioles. Fig. 113 represents a small portion of the tissue shown by Fig. 112, but more highly magnified. It makes even more evident the resemblance to an emphysematous bleb upon the surface of the lung. The central region contains enormously dilated tubules with broken walls, so that large cavities are formed. The epithelium is degenerated, and there is fibrous tissue scattered among the tubules. A Malpighian body with dilated capsule whose capillary loop is undergoing atrophy is included. The central region is entirely surrounded by fibrous tissue, and over it is the capsule of the kidney, which is thickened and raised above the general level,

while to right and left over the fibrous areas it is drawn downward by the contraction which is so common in fibrous tissue. The fibrous tissue is more dense than usual in the kidney, and hardly any trace of the normal elements composing kidney can be seen in it. It is likely that a kidney such as this was very unfit to perform its function, if it was not entirely useless. Substituting liquid contents for air, the parallelism of the appearance of this fibroid destruction of the kidney with that of pulmonary emphysema is so close that it can hardly be exaggerated. The parallelism also extends to the manner in which the two forms of disease have their origin.

Fig. 114 represents a transverse section across the entire kidney of a man of thirty-one who died of Bright's disease. It is an instance of extreme contraction of the kidney, being three-quarters of an inch across in the long and one-quarter in the short diameter. Of course it was not so small as this when removed from the body, as there is always some shrinkage in preparing tissue for section. The other kidney was much larger, but it also was extremely fibroid. It is difficult to imagine anything that would show better than this kidney does distortion of natural relations; there is no distinction into cortex and medulla, but a confused collection of fibrous tissue, fat, blood-vessels, and diseased renal tissue. The blood-vessels even with this low amplification can be seen to be greatly thickened, some of them almost closed. When more magnified they show a great variety of arterial disease, which is generally the case in fibroid and contracted kidney. The number of vessels in proportion to the area of tissue is very great, recalling to some extent the appearance of an angioma, but it must be remembered that this is a directly opposite condition, a retrogression, the result of shrinking instead of growth and increase, such as take place in an angioma. The increased proportional number of vessels is due to the fact that they are of such structure as to be difficult to destroy, and, while much of the renal secreting substance disappears in the course of contraction, the vessels, on the contrary, persist in very great numbers and are diseased and thickened. Such thickened and diseased vessels can under no circumstances be studied to greater advantage than in contracted kidneys, in which they are found presenting every kind of histological growth and destruction, and an infinite variety of changes of the relations and appearance of the three coats. Arteries are much more persistent in contracted kidneys than veins, and a great many more of them remain, or else this effect is produced by the fact that the veins have become so

FIG. 114.—CONTRACTED KIDNEY. (× 6.)

A transverse section across the entire kidney of a man of thirty-one years who died of Bright's disease. The capsule is greatly and irregularly thickened, and fibrous strands extend from it into the perirenal fat; it contains a good many blood-vessels. The fibroid Malpighian bodies and round-cell infiltration cannot be clearly distinguished with such low amplification. The arteries are very numerous and their walls greatly thickened. Quite large arteries are seen in the renal tissue itself. *w* is a portion of a calyx connected with the ureter. The proportion of fat to renal tissue is very large.

FIG. 114.

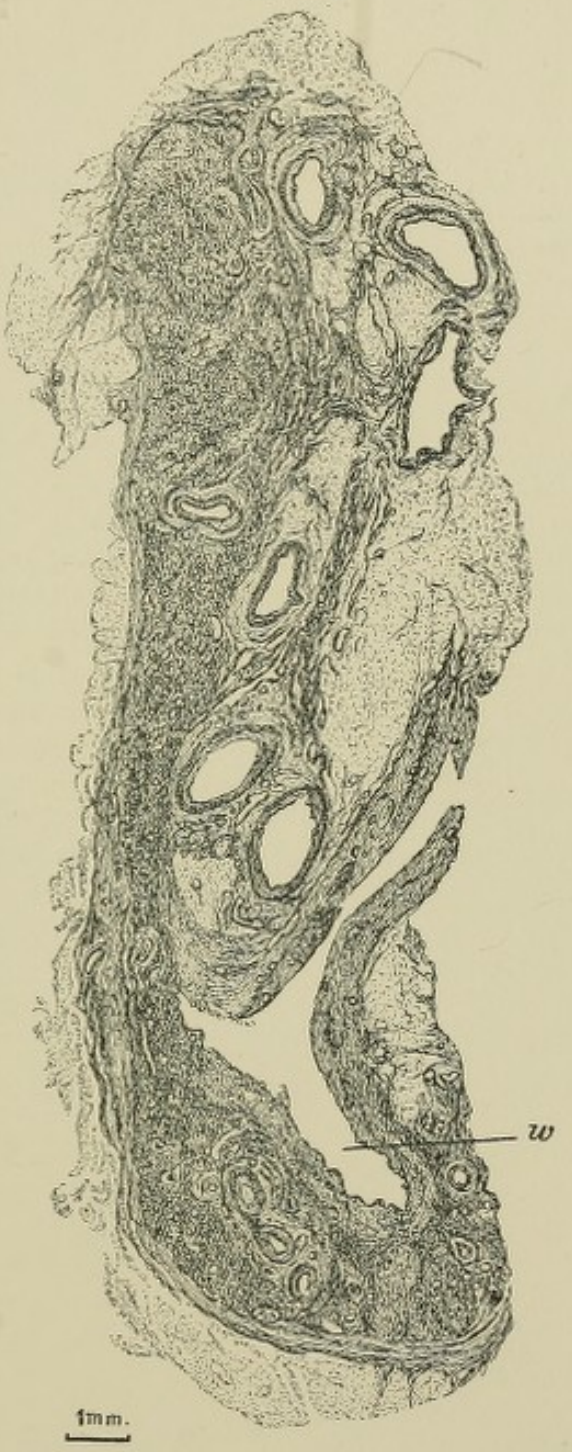
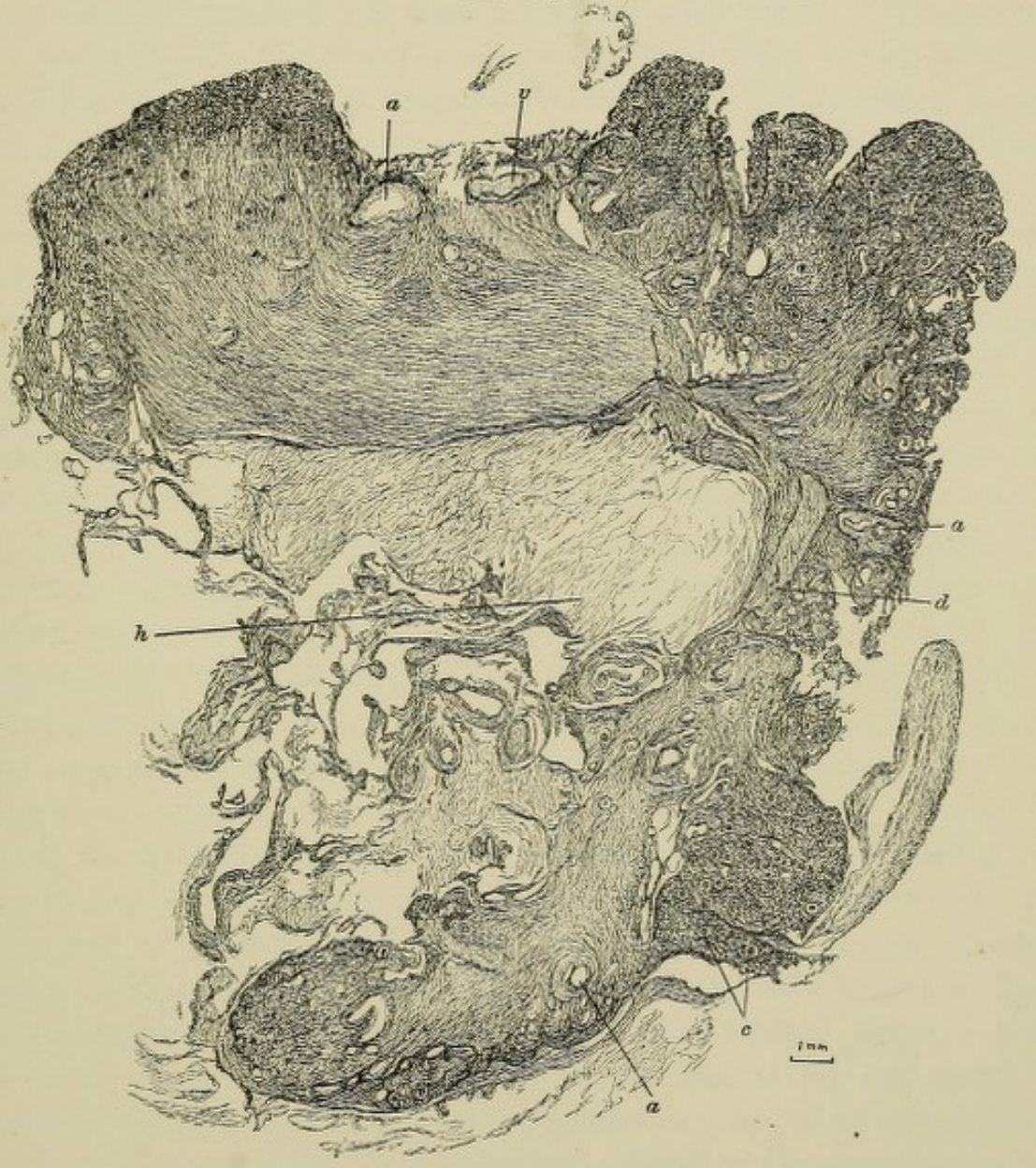


FIG. 115.—CONTRACTED KIDNEY. (× 4.)

Section across the kidney of a woman forty-two years of age who died of cerebral apoplexy. The direction of section is dorso-ventral, exhibiting the horseshoe shape. *a*, *a*, *a* are arteries, which are very numerous and some of them quite close to the capsular surface. Even with the low amplification it is seen that they are thick-walled. *v*, a vein containing clotted blood. *c*, Malpighian bodies, of which there are many close to the surface. They are almost all fibroid, but this can be distinctly seen only with greater amplification. *h*, the hilum, containing much fat, but made to appear larger than it was during life, for the two halves of the kidney spread apart somewhat in process of preparation. The hilum contains fat, blood-vessels, etc., and, although its size is exaggerated, it was quite large before the spreading of the two halves of the kidney occurred, and thus the organ appeared larger than it really was. *d* is an exceedingly narrow region. A noticeable feature is the irregular distribution of the contraction, the amount of tissue upon one side of the hilum being nearly twice as great as upon the other.

FIG. 115.



thickened by disease that they can no longer be distinguished from arteries. It is inconceivable that all the blood-vessels which existed in this kidney when it was of the full natural size are still present in the reduced organ which survived the disease, and it is therefore almost certain that the vessels which were destroyed contributed their part toward the formation of the fibrous tissue by having their openings entirely occluded and thus becoming solid cords. This belief is warranted by the fact that the whole tendency of the vessels is toward increase of their fibrous tissue, thickening, and finally entire closure, for it is not rare to see a vessel with its lumen entirely obliterated. The most striking feature of all, perhaps, shown by the drawing in connection with the blood-vessels is their displacement from their natural position. In natural kidney the vessels enter its substance at the junction of the cortical and medullary portions and quickly break up into small twigs, so that no large ones exist in the cortical substance near the surface. In this organ, owing to the distortion and dragging effect of the growing fibrous tissue, large vessels are seen in the secreting substance, and good-sized ones have been pushed so far from their natural position as to lie near the capsule. The portions of perirenal fat included contain many blood-vessels, a few of which are shown by the drawing. When it is studied with greater amplification it can be seen to contain many new blood-vessels of the kind that grow in tissues developed as the result of disease. Besides the evidence of a morbid condition afforded by the presence of these new blood-vessels, the perirenal fat is more fibrous than natural, and, what is especially notable, there are fibrous strands extending from the thickened and coarse capsule into the fat and firmly binding capsule and fat together, as is usual under the circumstances. Another feature exhibited by the drawing—and it is one which should always be considered in estimating the size of a contracted kidney—is that there is a great deal of fat in the hilum and about the ureter and calyces. This is a very common occurrence; and it is often the case that when there is but little secreting substance the organ is made to appear much larger than it really is by the stuffing of the hilum with fat. The Malpighian bodies are in all stages of fibroid degeneration, but it requires greater amplification to show this. The other kidney was cystic.

Fig. 115 represents a section across the entire kidney of a woman of forty-two who died of cerebral apoplexy. It is about one inch across in each of its diameters, and therefore was extremely con-

tracted. This kidney shows a condition in many respects similar to that of the last described, but it demonstrates irregularity of distribution of the contraction, the Malpighian bodies and blood-vessels having been pushed to the surface, and the organ appearing larger than it really was, owing to the filling of the hilum with fat. With regard to the irregularity of the contraction, a glance shows that the portion of kidney upon one side of the hilum is nearly twice as large as upon the other, and, further, that at the point opposite the opening of the hilum the secreting substance is reduced to such an extent that only a narrow bridge remains to join the two halves of the kidney together. Near this narrow part and elsewhere toward the capsular surface the blood-vessels and fibroid Malpighian bodies can be seen in great numbers lying so near as almost to touch the capsule. Into this position they were forced by the growth of fibrous tissue and shrinking of the organ, for, as has been said, in natural kidney large blood-vessels are to be found only at the junction of the cortex and medulla, and in the region directly adjacent to the capsule there are but few Malpighian bodies. The drawing shows distinctly that there was more fat than natural in the hilum, but at the same time it exaggerates this condition somewhat, for in course of preparation the two halves of the kidney were forced farther apart than they were during life. Such low amplification was used in making the picture that many details of structure fail to show which are easily distinguished when it is more highly magnified, as for instance in the portions rendered by long flowing lines.

Fig. 116 is from the kidney of a man of seventy who died of chronic myelitis and who had very contracted kidneys. It is to show a tubule exceedingly narrowed and deformed which lies isolated in the midst of fibrous tissue. The condition is parallel with what has been shown to occur in the liver in hypertrophic cirrhosis, under which circumstances a column of hepatic secreting cells may be compressed to such an extent as to look like a secreting tubule in the early stage of its embryological development. The reasons for believing this disease of the liver to be a retrogression owing to atrophy of the columns of secreting cells, and not a development of new bile-ducts as has been commonly supposed, have already been discussed. The kidney tubule is surrounded by fibrous tissue, no others being adjacent to it as in healthy kidney. At one end of it the epithelial cells have disappeared, and it appears to be composed of fibrous substance, while at the other the epithelial cells are squeezed together so that

FIG. 116.—RENAL TUBULE COMPRESSED BY FIBROSIS. (× 220.)

From a man of seventy years who died of chronic myelitis. *b* is a large secreting tubule; *c*, a capillary; *d*, the compressed narrow tubule. It lies embedded in fibrous tissue, and its cells are flattened from pressure. The contrast in size between *d* and *b* is striking. As the region shown is close to the capsule, it cannot be that the narrow tubule is one of the loops of Henle, which are naturally very small. The destruction by pressure here depicted resembles that shown in the liver by Fig. 83.

FIG. 117.—CALCAREOUS DEPOSIT IN THE KIDNEY. (× 105.)

From a man seventy years of age who died of chronic myelitis and who had contracted kidneys. The section was cut from the medullary region across one of the papillæ near its apex, and therefore includes the largest-sized tubules. *a* is an arteriole, while all the other large openings are tubules. *c* is calcareous deposit which is seen to lie in the tissue around most of the tubules and even in the wall of the arteriole (*a*). The kidney was exceedingly fibroid, and so changed by disease that none of the epithelial lining of the tubules remains. There was no calcareous material within the calibres of the tubules. The deposit of mineral matter in the tissue around a cyst in the liver is shown by Fig. 80.

FIG. 116.

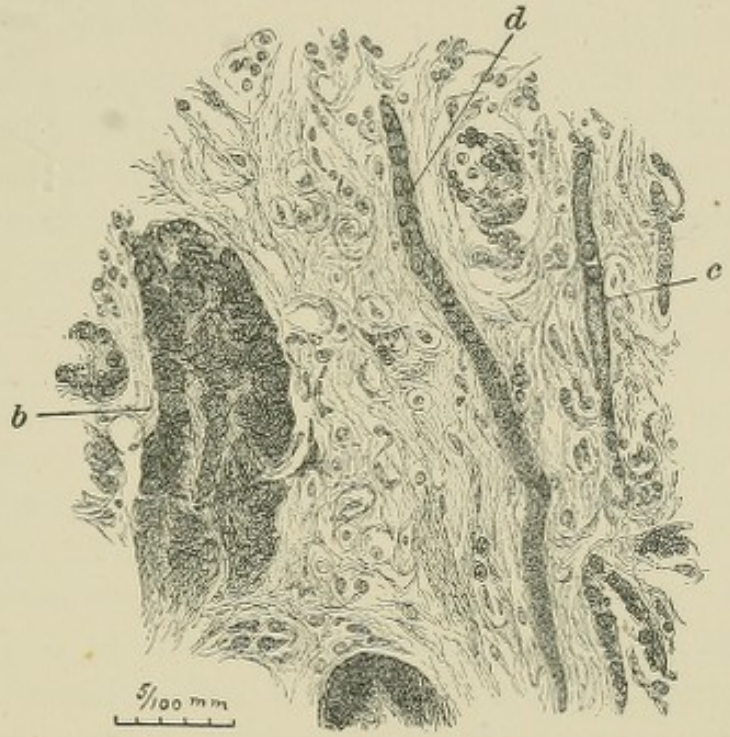
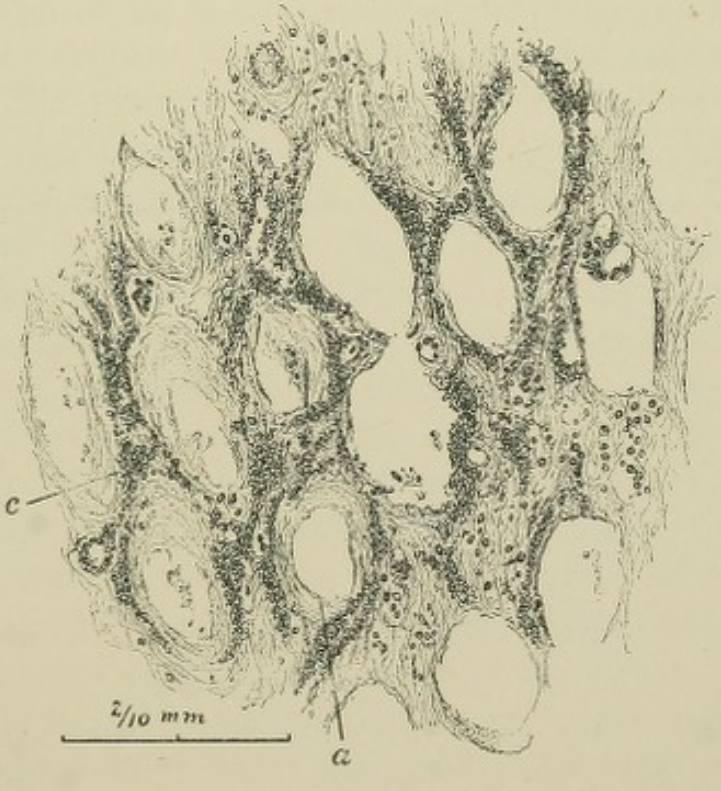


FIG. 117.



they lie in contact and the lumen of the tube is closed. The cells are so distorted that they are oval and their greatest diameter is parallel with the length of the tube. These cells are exactly like those which sometimes form the walls of cysts, as, for instance, in the spleen and kidneys (Figs. 97 and 123). This narrow renal tubule which was in process of atrophy is interesting, both because it shows one method of destruction of the secreting substance of the kidney during contraction, and because, owing to its striking resemblance to the atrophying cells of the liver (Fig. 83), it lends confirmatory evidence to the view that such things as these narrow shrunken columns of cells in the liver and kidneys are only parts of the great generalized process of fibrosis which goes on with the advance of years or in the young as a result of disease.

Fig. 117 is from the same section as the preceding. The purpose of the drawing is to show the early stage of the deposit of mineral matter in the kidney. This is of very frequent occurrence in contracted kidneys, and, as illustrations of the appearances are not included in any text-book of pathology with which I am acquainted, it seemed worth while to make a demonstration of the phenomenon. The drawing is of a section across one of the cones not far from its papilla, and it shows tissue so changed by the fibroid process that all trace of epithelial lining of the tubes has disappeared and the tubules appear as empty rings of fibroid tissue. The salt deposit lies in the tissue around the tubules and even in the wall of an arteriole (see description of plate), and it has had a tendency to dispose itself in rings around the openings rather than to be scattered loosely in disordered masses in the tissue. There is no mineral matter lying within the calibres of any of the tubules. For my own part, I have never seen mineral matter within the tubules after death, although it is so common an occurrence for patients to pass sand and concretions in the urine. Deposits such as those so well shown by the drawing are quite common in the kidney, and the deposit of mineral matter in the tissue around a small cyst in the liver has already been described (Fig. 80). Parrot * speaks of the deposit of urate of sodium in the collecting tubules of the medullary portion of the kidney as being a common occurrence in foundlings dead of marasmus. This I have never been able to find in any of the young infants that I have examined, although I have found deposits in the renal substance like those shown by the drawing, and mention has already been made of

* Clinique des Nouveau-Nés, L'Athrepsie, par J. Parrot, Paris, 1877.

a stone found in the kidney of an infant of six months. In the case of a stone of such size it would be impossible to ascertain where it originated, for in the course of its growth it would force itself into surrounding parts and break through the substance in which it lay at the time of its beginning.

Fig. 118 represents a portion of the kidney of a man thirty-two years of age who died of Bright's disease and heart disease. It is a type of one form of contracted kidney; there is fibrosis of the medullary portion to a greater degree than usual, and there is a small spot which is in many respects like a malignant new growth. The discussion of this latter feature will be taken up later. The general type of the fibrosis of the cortical portion is the same as that shown by Fig. 109, and its peculiarities need not be repeated. So far as concerns the medullary portion of the kidney it is hardly necessary to say that in cases of contracted kidney it bears its share in the process of disease, and becomes fibroid at the same time with the cortex. Extreme fibrosis of the medulla is shown by the illustration last described, and, as already stated, it was from the greatly contracted kidney of a man seventy years old. Besides the mineral matter in the tissue around the tubules and arteriole, which is its most peculiar characteristic, the changed condition of the whole of the renal tissue is striking. Natural kidney consists in largest part of epithelial elements, and through it there is a small amount of fibrous material which carries the numerous blood-vessels and affords a supporting framework for the tubules; but in this instance no epithelium is to be seen, and most of it is fibrous tissue poor in nuclei. This is no more, perhaps, than might be expected when it is recalled that it was the case of an old man with a kidney greatly reduced in size and excessively fibroid. The medullary portion simply partook in the general process of disease, and its epithelium atrophied and disappeared and fibroid tissue replaced it at the same time with the fibroid destruction of the cortex. Fig. 118 is an instance of fibrosis of another kind, for the patient was a man in middle life who died of a comparatively acute attack, and whose kidney, although contracted and fibroid, shows the disease under a very different aspect. The drawing shows that the medullary portion is fibroid, the amount of epithelium being much less than normal and that of fibrous tissue increased, but, as this also was an instance of contracted kidney with unmistakable disease of the cortex, it is not surprising that the medulla as well as the cortical portion should have been diseased. The way in which

FIG. 118.—GENERAL RENAL FIBROSIS, FIBROSIS OF THE MEDULLARY PORTION, AND A GROWTH RESEMBLING CANCER. (× 10.)

From a man thirty-two years old who died of Bright's disease and organic disease of the heart. *a* is the spot like cancer, and a portion of it is represented more highly magnified by Fig. 119. *b* is an area in the medullary portion which shows fibroid disease. The general character of the cortical portion is similar to that of Fig. 109.

FIG. 118.

contraction of the kidney begins by thickening of the capsule and a depression of the surface of the organ with the growth of fibrous tissue beneath has already been mentioned, and the process illustrated by Figs. 106 and 109, and it was stated that such is the commonest mode of origin of the disease. My studies, however, have led me to believe that fibrosis in some exceptional instances begins in the medullary portion. Occasionally at post-mortem examinations the cones will be found to be very light-colored, almost whitish, so that they present a very strong contrast in color with the rest of the kidney, and at the same time they are very hard to the touch. Several times when I have examined such tissue with the microscope I have thought the amount of epithelium less than normal and the fibrous tissue increased, and yet there was no discoverable disease of the cortex. Such a condition is difficult to be sure of, for the change is not a gross one, and it would be still more difficult to demonstrate. However, as the macroscopic appearances and the result of microscopical examination point in the same direction, I have been led to believe that sometimes fibrosis of the kidney begins in the medullary tissue.

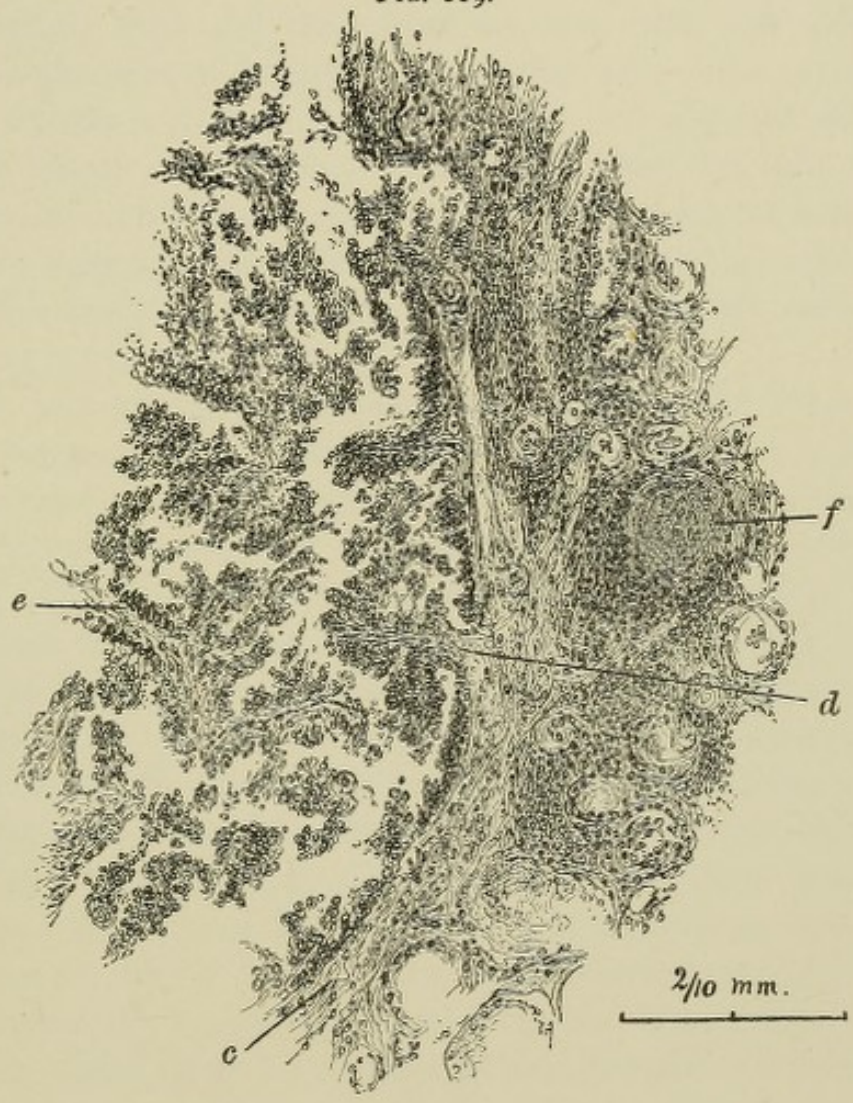
Fig. 119 represents a portion of the growth resembling cancer, the whole of which is included under less amplification in Fig. 118. (See description of Fig. 118.) It has already been said that the case was one of Bright's disease and heart disease in a man of thirty-two. The patient died having dropsy and dyspnœa and a typical development of all the symptoms which are common to such a condition. At the post-mortem examination there was nothing found resembling cancer except the one minute spot in the kidney, nor did the microscope reveal the existence of anything of the kind, although sections of the heart, aorta, lungs, liver, and spleen, as well as of the kidney, were examined. The drawings show so far as concerns the growth a condition of affairs foreign to contraction of the kidney, of which the case was a typical instance. The growth is seen in the low-power picture to be a little more than one millimetre across, and sections of it were made in more than one direction, which showed it to be spherical. There is a distinct wall around it separating it from the renal tissue. The high-power drawing shows the details of structure: its capsule is formed of fibrous tissue, and from it spring cauliflower-like growths composed of a fibrous stem with columnar cells arranged upon each side. Other similar fragments lie loosely in the central mass. These also probably grew from the fibrous capsule, but were separated from it in cutting the section. The general mass of the central portion of

the growth is composed of cells and fibrous shreds which are so degenerated in many places as to have no distinct outlines. According to accepted pathological classifications, the growth must be placed with the neoplasms, for such tissue is not known to have a natural home in the kidney, and the cauliflower growths springing from the fibrous capsule are strikingly like some forms of cancer. An easy escape from the difficulty of explaining what the growth really was and how it arose is to assume that it was cancer, and that others of similar nature existed in the body of the patient, but were not found for lack of sufficient search, or that this was the beginning of cancer and if the patient had lived a little longer it would have shown its well-known malignant nature by the enlargement of the primary growth and the development of secondary growths. Such an assumption is not warranted by the facts. Among surgeons of large experience there have always been many who believe that a blow may be the determining cause of cancer of the breast in a woman, or the excessive use of a pipe of cancer of the lip or tongue. On the other hand, it is generally accepted as a fact that cancer is in some way of a specific nature and that its spread is due to an infectious quality,—that the metastases are due to infection of the more distant parts by the primary tumor which is assumed to be the centre from which all the other growths arise, and to be their cause. The beliefs that cancer can be induced by an irritant or by injury and that it is a specific disease of an infectious nature are irreconcilable. To say that some individuals are of such nature that their bodies present a fertile soil in which the specific seed of cancer will grow readily while others are sterile is to drive too far the parallel with agricultural conditions. It is well known that many plants which will flourish in one soil will hardly germinate, much less grow, in others, but this homely agricultural truth has been used to explain difficulties and to overcome irreconcilable facts in human pathology until it is difficult to hear it with patience. To accept it in regard to cancer it is necessary to believe that in those capable of having the disease the seed must always be lurking in the system, ready to break out as soon as the requisite irritation is supplied. It involves the assumption in the first place of the specific and infectious nature of cancer, that it is of extraneous nature, a something that attacks the body from without, and that it can in no wise be due to deformity or misdirected growth of the natural tissues. Such a method of inference is that of the weak or specious logician who, having assumed his premises, proceeds to draw

FIG. 119.—GROWTH IN THE KIDNEY RESEMBLING CANCER. (× 105.)

Part of the region *a* in Fig. 118, more highly magnified. *c* is the fibrous capsule which surrounds the growth. To the left of this is the new growth, and to its right fibrous renal tissue. *f* is a fibroid Malpighian body, and about it is the fibrous renal tissue, showing much round-cell infiltration. In the new growth, *d* denotes a cauliflower excrescence which springs from the fibrous capsule, and *e* a loose shred of organized tissue. *d* and *e* are of similar structure, being composed of a central fibrous strand with columnar cells set upon both sides. They much resemble some of the forms of epithelial cancer.

FIG. 119.



conclusions without stopping to ascertain that the premises, which are the foundation of the structure, are correct. The theory is so complicated, and involves so much that cannot be explained by the laws governing the growth of vegetables, from which the simile of the fertile soil was derived, that one is warranted in declining to accept it. In the discussion of lesions of the blood-vessels it has already been shown (Fig. 38) that growths are sometimes found in the walls of vessels presenting some of the physical characteristics of cancer but which certainly were not cancerous, and attention was called to the fact that in the skin of infants the epithelial cells often arrange themselves in whorls which are similar to the cell-nests of skin cancer. These two instances show that it is possible for the cells to arrange themselves in such a way as to produce an imitation of cancer. It is much more reasonable to believe that the tumor in the kidney was the result of misdirected cell-growth and that it imitated cancer than to believe that it was cancerous.

Fig. 120 is from the kidney of a woman sixty-one years old who died of dysentery and Bright's disease. The capsule is very thick, the tubules are somewhat dilated, and the epithelium is degenerated, having lost its sharpness of outline and characteristic columnar appearance. The purpose, however, for which the drawing was made was to show the condition of three Malpighian bodies, which are included and which demonstrate increasing gradations of fibrosis. (See description.) In the one least diseased Bowman's capsule is very much thickened, the thickening being of the inner surface and having occurred in such a way as to reduce the space for the capillary loop, which is still very distinct, although not more than one-third the natural size. Outside of Bowman's capsule there is an area of round-cell infiltration, which denotes that inflammation constituted a part of the process of fibrosis. At this stage the Malpighian body is of normal size, being about two-tenths of a millimetre in diameter. The Malpighian body in the second stage of fibrosis is reduced in size by about one-fourth, being between one-tenth and two-tenths of a millimetre in diameter. Its Bowman's capsule is of the same degree of thickness as the first one, but the space for the capillary loop is smaller, and the loop itself is no longer recognizable as a capillary, being reduced to a mere ball of fibrous tissue of slightly different appearance from Bowman's capsule, with which it is in contact. The body is surrounded by an area of round-cell infiltration which is much more extensive than that around the first one. In the third stage of fibrosis

the Malpighian body has entirely lost its character, and is nothing but a little fibrous ball which is only one-tenth of a millimetre in diameter, and therefore reduced in size by one-half. It is not even surrounded by an area of inflammation. If these three Malpighian bodies constitute a type of fibroid destruction, the process consists of thickening of Bowman's capsule and inflammation of the surrounding tissue. In this process of disease the capillary loop does not appear to take any very active part, although in the second stage it has been converted into a fibrous mass which was probably entirely impermeable to the passage of blood. Inflammation is considerable in the first stage, is still more extensive in the second, and has almost entirely faded away in the third.

Fig. 121 shows a condition of the capsule of the kidney which is common and characteristic of renal fibrosis. The section is from a man of forty-eight who died of dysentery and had fibroid and cystic disease of the kidneys. A casual glance at the drawing might lead one to say that it represents renal tissue and an unnaturally thin capsule with perirenal fat adherent to it. Exactly the contrary, however, is the real explanation of the appearances: the capsule is greatly thickened, and its layers have been torn apart so as to form wavy lines and cavities. Some of the cavities are circular, and they resemble to a limited extent fat cells. A moment's consideration, however, should be sufficient to satisfy any one that the tissue is not fat. The cavities are larger than ordinary fat cells, and the fibrous tissue and its arrangements are such as to make it certain the material is not fat. Perirenal fat is not very different from other forms of fat, and an example of its appearance is exhibited by Fig. 110, which, however, is not typical, as it is more fibroid than natural. The irregular cavities and thick shreddy fibrous material shown in the drawing suggest the explanation that some liquid or semi-solid material had been effused into the substance of the capsule and had forced its parallel layers apart. As already said, this condition of the capsule is common in fibroid kidney, and its existence gives rise occasionally to a curious anomaly. It is well known that generally in cases of fibroid, and especially in granular kidney, when the surface is uneven the capsule is more tightly adherent than natural. A peculiar condition in cases of granular kidney is that it often seems nearly impossible to remove the kidney from the body with the capsule still upon it. Careful investigation in such instances has revealed that the whole of the capsule was not pulled off, but that a thin layer of it, as is shown in the drawing, remained ad-

FIG. 120.—FIBROID KIDNEY. (× 50.)

From an elderly woman who died of dysentery and Bright's disease. *c* is the capsule, which is very thick; *h* is a loose shred of capsule; *d*, *e*, and *f* are Malpighian bodies in different stages of fibrous destruction. *d* has a leaf-shaped remnant of the capillary loop and a thick fibrous capsule. *e* has at its centre a remnant of the capillary loop which is surrounded by the thickened fibrous capsule of Bowman. *f* is a small fibroid ball. All three are surrounded by areas of round-cell infiltration.

FIG. 121.—SHREDDED AND THICKENED CAPSULE OF KIDNEY. (× 50.)

From a man of forty-eight years who died of dysentery. The layers of the capsule have been torn apart by liquid which filled the apparently empty spaces. It is impossible to suppose this was fatty change, for Fig. 110 shows perirenal fat, and the contrast in appearance is very great.

FIG. 120.

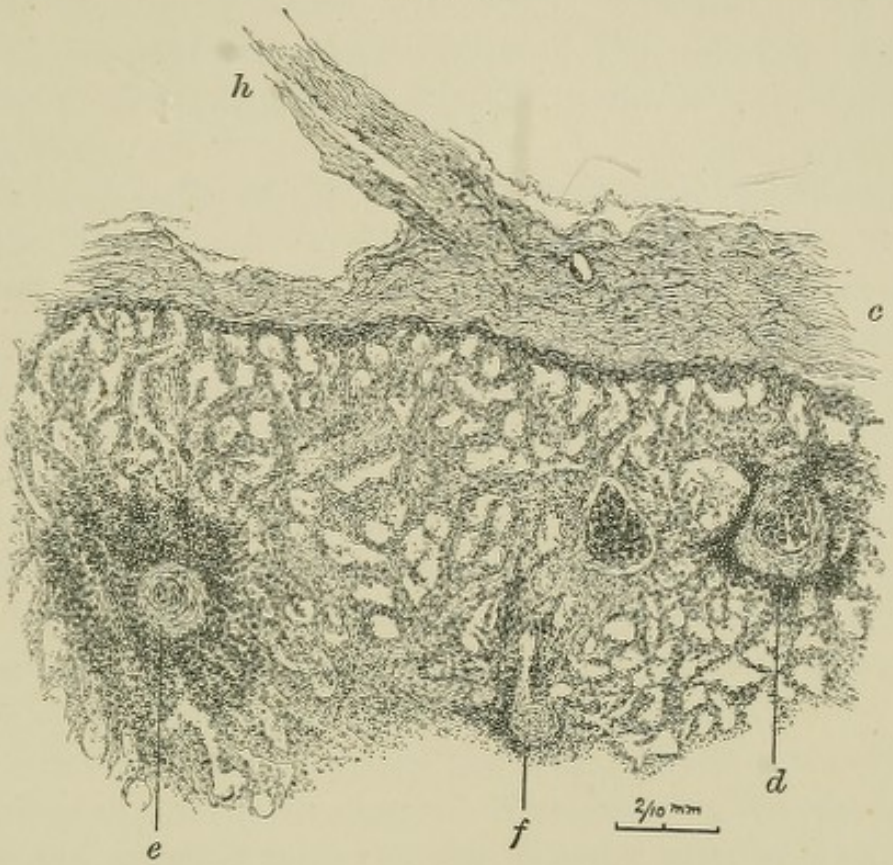
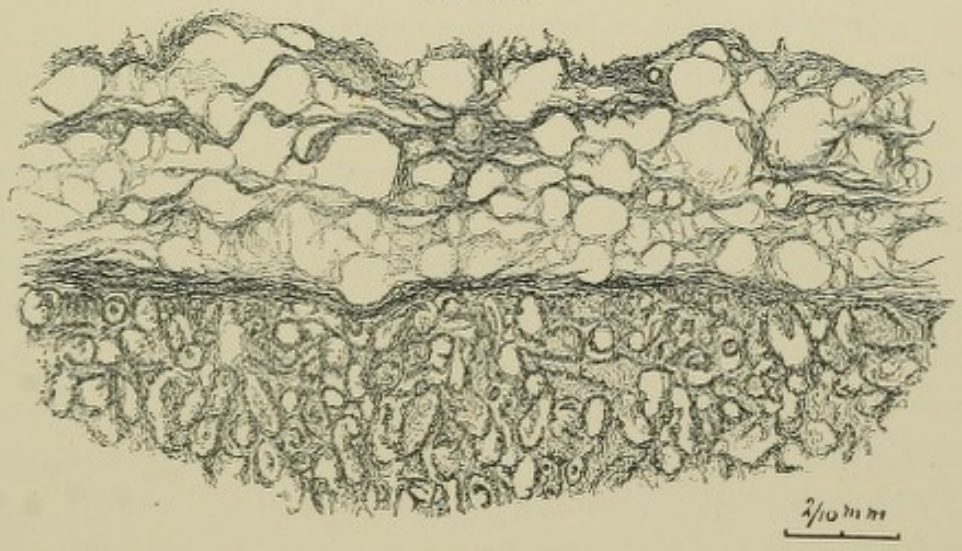


FIG. 121.



herent to the kidney. This effect is due to the separation of the capsule into two layers, the thicker of which is torn off with the perirenal fat, leaving a thin layer upon the kidney. To the naked eye it appears as if none of the capsule is left, and only microscopical examination demonstrates the fact that a part of it remains adhering to the kidney.

In no other organ of the body are cysts known to be so common as in the kidney, and the characteristics of renal cysts have therefore been very closely studied. Although such is the case, there remains a great deal to be learned in regard to them, and even yet there is much difference of opinion about some of their peculiarities. It has sometimes been said that cysts in the kidneys of the aged are not under all circumstances to be considered as evidence of disease. Such a belief has always seemed to me as untenable as would be the position of one who should assert that cavities in the lungs are not always to be attributed to disease. Renal cysts must under all circumstances be either congenital or due to disease which has destroyed portions of the kidneys to make room for the cysts.

Fig. 122 represents a cyst of the kidney from a man of fifty-two who died of organic heart disease. The cyst lies directly beneath the capsule, and across it are a number of lines, some of which are complete, crossing the cavity from side to side, while others reach only part way across. These lines, for as such they appear when seen in section, are portions of partitions and shelves which divided or partially divided the cyst-cavity. The cavity of the cyst was therefore composed of a number of chambers, some of which were completely separated from one another, or again the chambers communicated because they were only partially separated by shelves. It is an exceedingly common characteristic of cysts of the kidney to be subdivided as shown by the drawing. The partitions when seen with the naked eye appear as thin membranes of delicate texture. If there is one particular in regard to which cysts differ more than another, it is in the nature of their walls. In the cyst under consideration the cavity was hollowed out of the renal tissue directly, and there is no differentiated wall, but the cyst-contents lay in contact with the kidney tissue. This is shown by the drawing, but is made even more striking by Fig. 123, which is an enlarged picture of a portion of the same tissue more highly magnified. In it there is no trace of anything like a fibrous cyst-wall. A Malpighian body is included which lay in one of the partitions. The Bowman's capsule of this is somewhat thick-

ened, but the capillary loop remained in a fairly good state of preservation. The cells forming one of the shelves are very like some cells which have already been depicted as existing in the wall of a cyst of the spleen. There is every reason to suppose that these cells which are so unlike the ordinary columnar secreting cells lining most of the renal secreting tubules have simply been modified by their changed conditions and surroundings, and that there has not been anything like a new growth.

Fig. 124 is from the kidney of a man of about sixty who died of illuminating-gas poisoning and was found to have pulmonary phthisis and cystic disease of the kidneys. The drawing is of a portion of tissue bounding a cyst, and it shows that the cyst-wall is composed of a thick layer of fibrous tissue. The renal tissue adjacent to the cyst-wall is fibroid, there being Malpighian bodies which have been converted into mere fibrous balls, and others around which the capsule of Bowman is fibroid and thicker than natural. Throughout the whole of the tissue there has been a growth of fibrous material to such an extent that were it not for the Malpighian bodies it could hardly be recognized as kidney. The contrast between this picture and the preceding is very striking in that the one cyst has such a distinct fibrous wall and the other is a cavity hollowed out of the tissue. It is strange that it should be possible for cysts to differ so far, although there is every reason to suppose the process is the same in the two cases, the presence or absence of a fibrous cyst-wall signifying only variation caused by difference of the circumstances under which the cyst grew and the condition of the tissue.

Fig. 125 represents diseased kidney which is interesting for more than one reason. The case was one of hydronephrosis in which the kidney was almost entirely destroyed. Nothing is known of the history of the patient. There are four good-sized cavities, a larger one and below it three smaller ones, which it would seem can be classified only as cysts. All the cavities are nearly filled with structureless solid material, and the walls are formed of cells like those of epithelium. Scattered through the tissue are numerous renal tubules containing casts. The cysts and tubules are similar in all respects except size; the cyst-contents and the casts in the tubules are alike, and the cells of both present the same appearance. These cells are little like healthy renal epithelium, but the situation they occupy shows that they certainly are renal secreting cells. Their appearance is almost exactly the same as that of some of the cells in Fig. 123, which, however, are twice as

FIG. 122.—RENAL CYST WITHOUT FIBROUS WALL. (× 6.)

From a man of fifty-two years who died of organic heart disease. *c* is the capsule. The cyst is large, irregularly shaped, and directly underneath the capsule. Across it pass several lines. These lines are parts of membranes which formed shelves and partitions irregularly dividing the cyst into separate or partly separate chambers. The cyst-cavity contains some amorphous material and loose shreds. *d* denotes the region shown more highly magnified by Fig. 123. At *d* is a Malpighian body almost uncovered in the cyst-cavity. There is nowhere any differentiated cyst-wall; the contents of the cyst lay directly in contact with the kidney tissue.

FIG. 123.—RENAL CYST WITHOUT FIBROUS WALL. (× 105.)

The region *d* in Fig. 122, more highly magnified. The same relative position has been maintained. The Malpighian body is here *b*, and it is seen to form part of one of the shelves (lines) seen in Fig. 122. *e* and *f* are in the cyst-cavity, and *c* indicates a part of one of the shelves in which the cells are large and oval. It looks like kidney tissue altered by its changed surroundings. The cells at *c* closely resemble those shown as forming the wall of a cyst in the spleen in Figs. 96, 97, and 98. There is nowhere any fibrous cyst-wall, kidney tissue forming the boundary of the cyst. *a* is an arteriole with thickened fibrous walls.

FIG. 122.

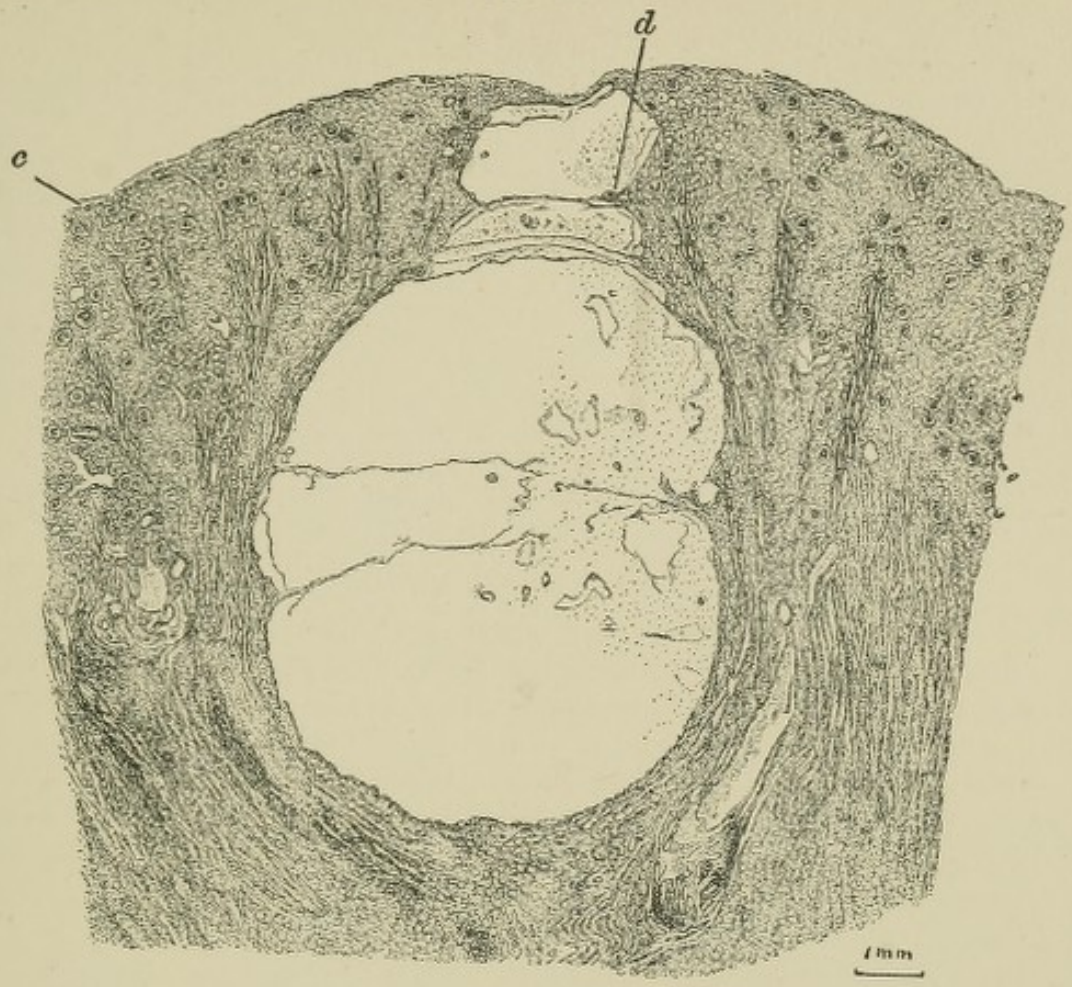


FIG. 123.

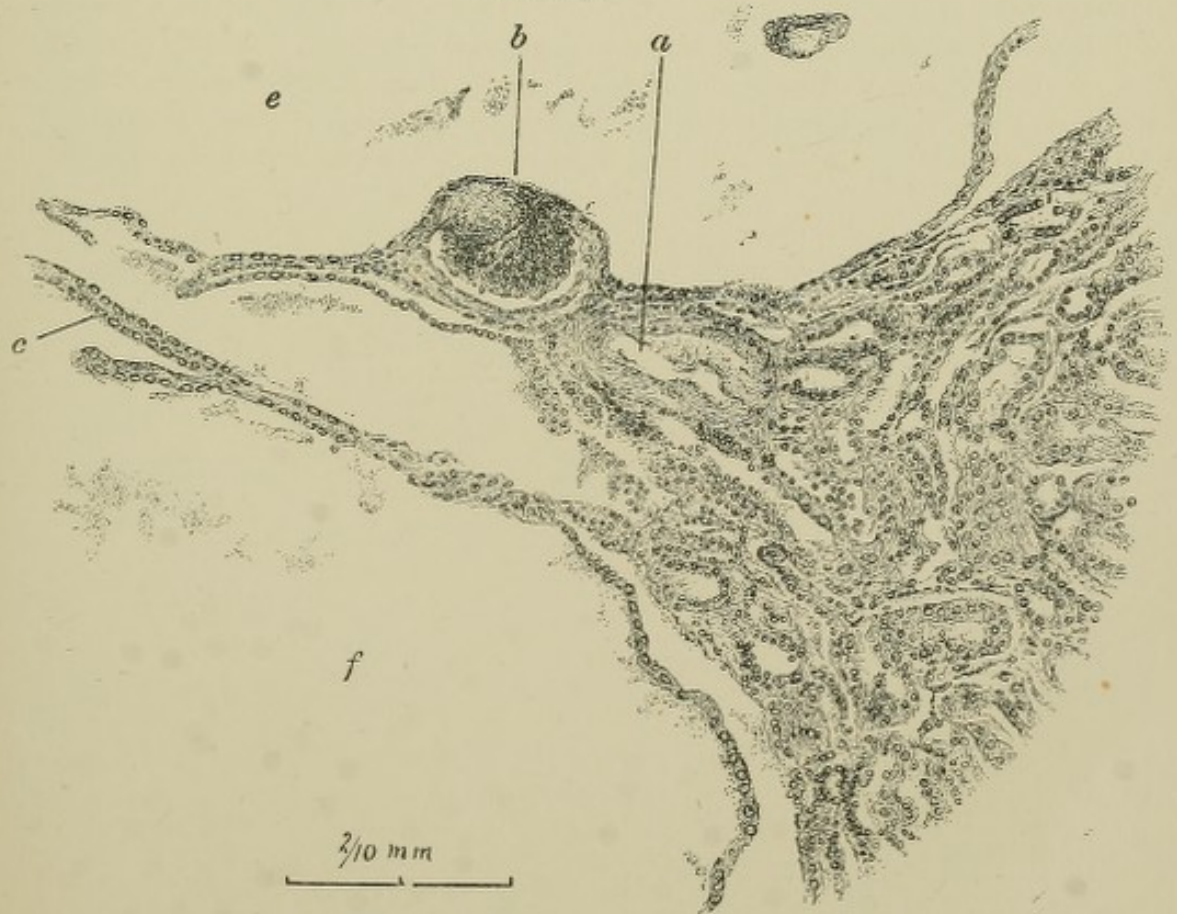
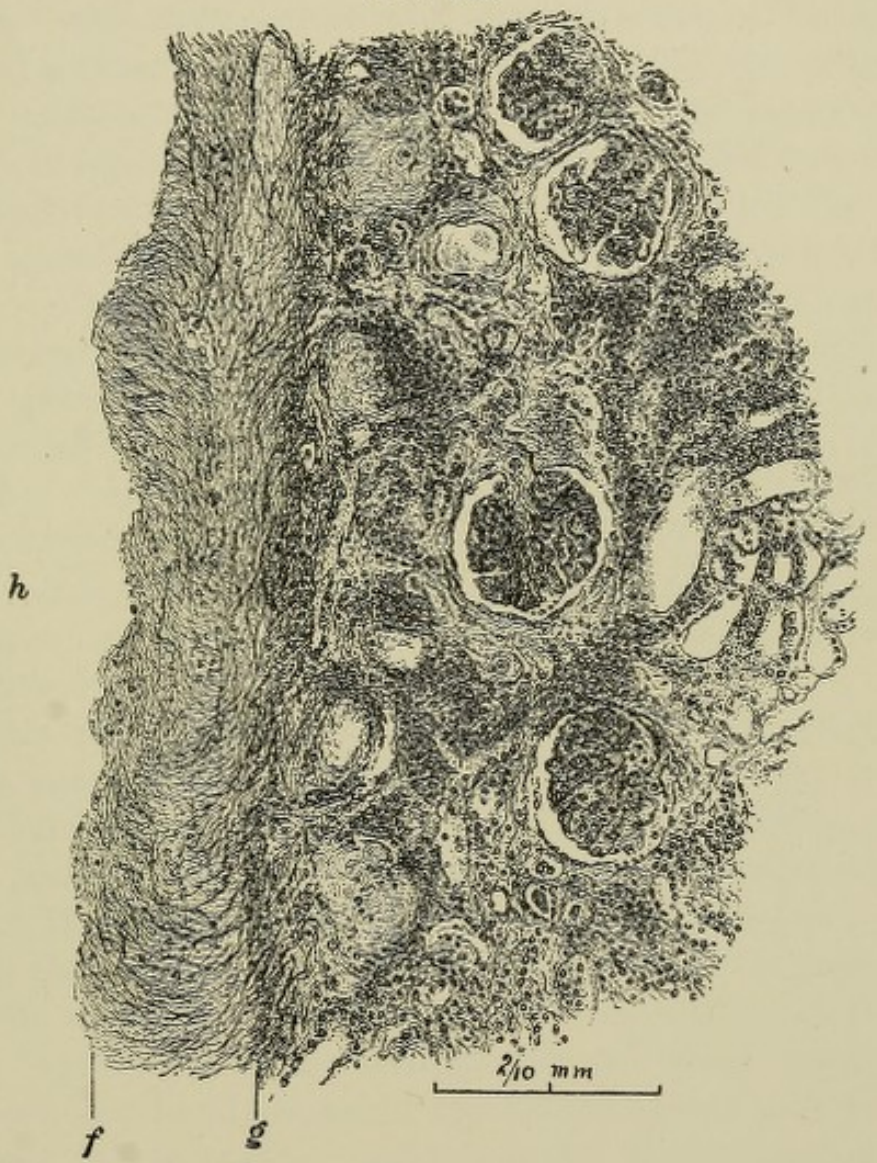


FIG. 124.—RENAL CYST WITH THICK FIBROUS WALL. (× 105.)

From a man of about sixty years who had phthisis and cystic kidneys and died of illuminating-gas poisoning. The drawing is of a portion of the wall of a renal cyst, and is to be contrasted with Fig. 123. Between *f* and *g* is the thick fibrous membrane which formed the wall of the cyst. *h* is placed in the cyst-cavity. The renal tissue is fibroid, and there is round-cell infiltration.

FIG. 124.



much magnified. The disease is to be explained only as an early stage of cystic degeneration. Whether such dilated tubules would have undergone further enlargement, thus forming the ordinary cysts which are of such frequent occurrence, cannot be known. Cavities like those described are not rare in cases of extreme contraction, and there were a good many of them in the kidney represented by Fig. 114, but the amplification used in making the picture was not sufficient to show them. At the stage under consideration the cysts are always filled with structureless solid material, which, as has been said, appears to be exactly like the casts in the undilated secreting tubules. It is not unlikely that the growth of the casts has something to do with the production of the cysts. If such dilated tubules as those depicted, which have grown so much larger than natural that they are correctly classified as cysts, ever develop into ordinary cysts, they must undergo great modification. Ordinary cysts, as has been shown, sometimes have fibrous walls and again have no differentiated walls, and they generally contain a clear thin fluid, although sometimes there is semi-solid material in them. Cysts such as those shown by the drawing, which by their appearance still clearly demonstrate their origin in dilatation of the tubules, are always filled with solid material like casts, and have a boundary of epithelial cells, which, however, have been so modified as to have lost all resemblance to healthy kidney epithelium.

Fig. 125 presents, besides the cystic dilatations of the tubules which have been under discussion, other peculiarities which are of great interest. There are two amyloid arterioles, and the capsule, which is thick, has been thrown into wavy folds and has a homogeneous glassy appearance like amyloid material. This latter condition is not shown so well by the drawing as might be desired, for it is impossible to produce the effect with pen and ink, but the section itself is most striking. The arterioles are exactly like the vessel represented in Fig. 126, which is in all respects a typical example of amyloid disease. It is singular that in a case of hydronephrosis there should be amyloid disease of the blood-vessels and this peculiar condition of the thick and fibrous capsule of the kidney, which I believe is only another form of amyloid change. The case was in no way one which would ordinarily be classed as of amyloid disease. It has so frequently happened to me, however, in cases of chronic disease of the kidney involving extensive growth of morbid fibrous tissue, to find more or less of this homogeneous glassy material, which when it exists in

large deposits is named amyloid degeneration and is supposed to be the result of a special process of disease, that I have been driven to the belief that amyloid deposit is only a form of fibrous tissue in which there are few nuclei and great quantities of structureless substance.

Fig. 126 is from a section typical of amyloid disease of the kidney, and its appearances lend support to the foregoing explanation of amyloid degeneration. When portions of any of the organs are destroyed by chronic disease the natural tissue is to some extent replaced by fibrous tissue. Morbid fibrous tissue is not exactly like healthy fibrous structures, and, being the result of a destructive process, it is hardly to be expected that it should be. It differs so much at different times and under differing circumstances as to make it seem unreasonable to call it always by the one name of morbid fibrous tissue, and yet, upon closer consideration, even when two varieties of it seem most dissimilar it is impossible to avoid the conclusion that it is the same thing. Morbid fibroid tissue may grow in the liver, spleen, or kidney in a manner so latent that no change is at any time discoverable except an increase of the fine, nearly structureless framework of the organ. There may be no apparent activity of life in the affected part and no new growth of cells, but the process goes on until there are large bands of fibrous material poor in nuclei running through the tissue, destroying part of it to make room for themselves. Such is the latent form of fibrosis. On the other hand, when irritation and inflammation are active, any of the tissues may be so overwhelmed by infiltration as to be unrecognizable and appear as a confused and crowded mass of the round cells of inflammation. These two extreme forms of fibrosis, the bands of almost structureless fibrous tissue poor in nuclei, and the areas of round-cell infiltration, are so different that at first sight it is difficult to believe they can even be related, much less only varieties of the same disease. In the case of round-cell infiltration, however, if the disease goes on, and suppuration does not ensue, time will reduce the inflammation. As this becomes less active, the cells disappear, and their place is taken by fibrous tissue. As the cells become fewer and the fibrous or structureless material increases, it is evident that through the process of inflammation with its cell activity the same goal is reached, the destruction of the natural tissue of the organ and its replacement by morbid fibrous tissue. Both roads lead to the same end, the formation of common morbid fibrous tissue.

FIG. 125.—SMALL RENAL CYSTS AND AMYLOID DISEASE. (× 50.)

From a case of hydronephrosis. The kidney was atrophied and so changed that it was almost beyond recognition. The drawing includes the whole depth of the thickened capsule and tissue beneath. There is a good-sized cyst adjacent to the capsule, and directly beneath it are three smaller ones. All the cysts contain structureless solid material, and around this in each instance is a complete circle of cells unlike the epithelium of renal tubules. *t* is a tubule containing a cast, and there are many others of similar nature near it. These tubules containing casts are almost exactly like the cysts except in size. The cells both of the tubules and of the cysts are unlike healthy renal epithelium. Much of the tissue included in the drawing is fibrous, and it is doubtful if any of it could have been recognized as kidney from its appearance alone, so greatly has the disease changed it. *a*, *a* are two minute arterioles with walls thick and homogeneous, and their calibres small; they are exactly like amyloid vessels. *g* is the lower border of the capsule. The capsule is thickened and of peculiar structure, being thrown into wavy lines and having a homogeneous glassy appearance like amyloid deposit. This glassy tone cannot be very well shown in a pen-and-ink drawing.

FIG. 126.—AMYLOID ARTERIOLE AND MALPIGHIAN BODIES OF THE KIDNEY. (× 50.)

From a section of amyloid kidney. Nothing is known of the patient. *y* includes an amyloid arteriole (*a*) and an amyloid Malpighian body, both being surrounded by fibrous and infiltrated tissue. *z* is another amyloid Malpighian body. Its Bowman's capsule is thickened and fibrous, and outside of it the tissue is fibrous and infiltrated. In this Malpighian body the various turns of the capillary loop are still distinct, while in *y* the capillary has melted into an almost even amyloid mass. The structure of this typical amyloid deposit, both of the Malpighian capillaries and of the arteriole (*a*), is very like some material in the foregoing picture, and in the ileum represented by Figs. 104 and 105.

FIG. 125.

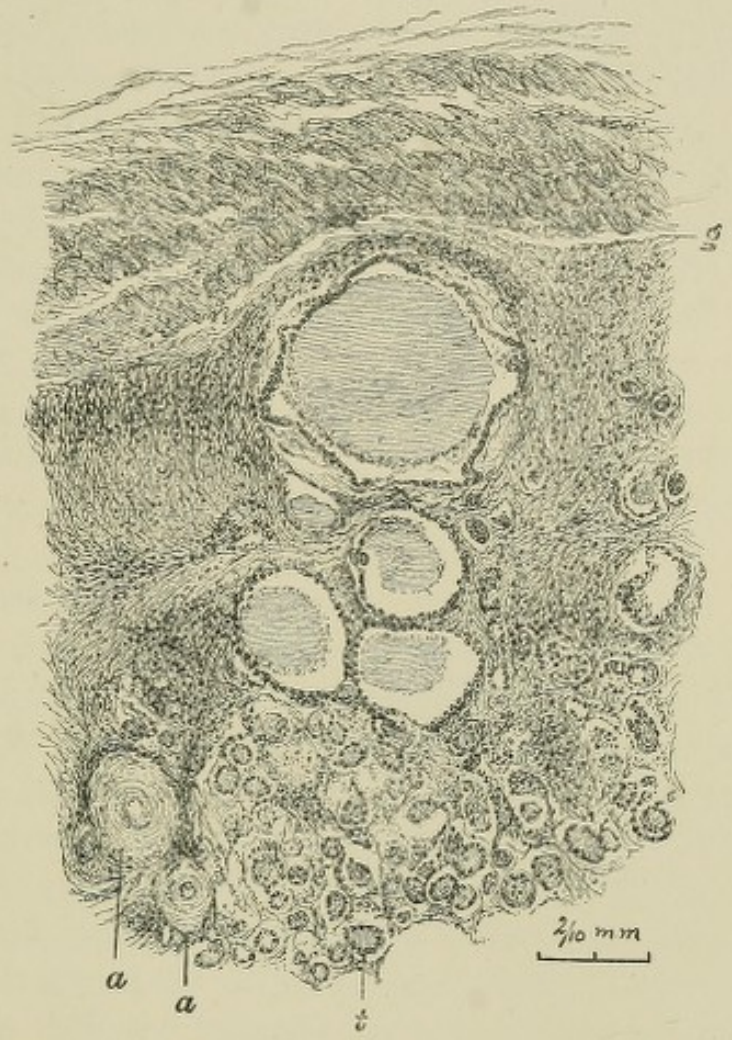
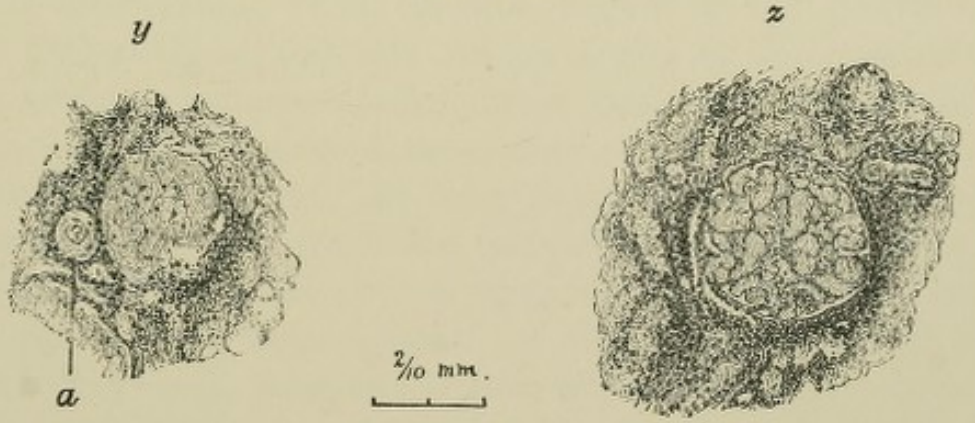


FIG. 126.



In what respect is the amyloid deposit different from some of the forms of morbid fibrous tissue? It does not seem reasonable that it should be given a name for itself and be supposed to be a heterogeneous product in the body simply because it turns brown when stained with iodine. There is nothing in the appearance of Fig. 126, either in the Malpighian bodies or in the arteriole, which is not more satisfactorily explained as being due to fibrous growth than by the assumption that some new and heterogeneous material was deposited in the walls of the Malpighian capillary and of the arteriole. There is a general great excess of the fibrous tissue of the kidney, besides the changes in the arterioles and Malpighian bodies, and this is always the case in amyloid disease, general fibrosis of the organ affected being as much a part of the process as the deposit of the amyloid material itself.

Before dismissing the subject of the kidney, some points which have not yet been touched upon must be brought out, and certain relations to one another of disease conditions already mentioned must be noticed. In what has been heretofore said it has been my intention to emphasize the fact that of all diseases of the kidney there is none so common and therefore none so important as fibrosis. Fibrosis is as inevitable to age as wrinkles of the skin, and its extent and distribution have great influence upon acute diseases, because fibroid organs are much more liable to inflammation than healthy tissue. Three different phases of fibrosis of the kidney are demonstrated by Figs. 109, 110, and 112, and they present both points of resemblance and of contrast. There are other varieties of the disease, of course, besides these three, and some such are exemplified in the series of illustrations. The essential feature is the production of morbid fibrous tissue, and this always grows at the expense of the natural secreting substance. An almost invariable accompaniment is thickening of the capsule of the kidney, and with it unnatural adhesion to the perirenal fat. In cases in which the fibroid deposit is irregularly distributed there are generally depressions making the surface of the kidney uneven. Among the illustrations are included examples of each of these lesions. A striking peculiarity of fibrosis of the kidney—and the same is true of fibrosis of other organs—is that in most instances it seems to begin near the surface, the capsule and the superficial portion of the kidney being first involved. Why this should be so is not at present understood, but that such is the case there cannot be any doubt. To return, however, to the three

illustrations. In Fig. 109 the capsule is thick, but part of it is much thicker than the rest, and is depressed below the general level, so that there was a pit upon the surface of the kidney. Beneath the thickest and depressed portion of the capsule the renal tissue has lost its ordinary appearance and has been converted into a mass of morbid fibroid tissue, which is rich in the round cells of inflammation and has scattered through it a few shrunken and fibroid Malpighian bodies. From this diseased region beneath the capsule fibroid bands extend in various directions through the kidney. The tubules are dilated and the epithelial cells somewhat degenerated, but most of the kidney tissue has not sustained great structural change. The effect, then, of the picture is of kidney the greatest part of which is composed of natural tissue, but through which ramify fibrous bands which in their growth destroyed secreting substance. The most striking feature, however, is that it looks as if the whole morbid fibrous process had had its origin in the thick and depressed portion of the capsule and subcapsular fibroid mass, and that from this region as a centre the fibroid tissue had grown in various directions. In Fig. 110 also the capsule is thick, and from it extend fibrous bands into the perirenal fat, which contains more fibrous tissue than healthy fat. The appearance of the renal tissue itself is in marked contrast with that last described: there is nothing like natural epithelium to be seen, but the tissue presents the effect of a smooth, almost structureless, basis material in which are scattered Malpighian bodies and tubules, some of which have been cut lengthwise and others across. In contrast with the previous picture, which was of comparatively healthy kidney seamed in various directions by disease, this one is everywhere diseased, with only scattered remains of the natural elements in it. Fig. 112 is diseased to an even greater degree, for if it were not for the Malpighian bodies which remain it could not be recognized as kidney. The capsule is thick, as in both the others. The greatest portion of tissue included is composed of heavy fibrous material, rich in cells, and through this are scattered open spaces formed by dilated and broken tubules. Except that the spaces which appear empty must have been filled with liquid instead of air, the parallel in appearance and mode of production with emphysema is exact. It is impossible to escape from the conviction that the process is the same in lung and in kidney, modified by the differences in the nature of the tissue of the two organs.

Extensive fibrosis of the kidney often exists and yet fair or even

good health is maintained. This must be because while portions of the kidney are destroyed by the fibroid growth others are left uninjured, and it explains why it so often happens that in persons who have died of other causes extensive disease of the kidney, which had not been suspected, is found after death. As has been already said in regard to other organs, it is probable that such latent disease is often in some way the determining cause of acute attacks. When such acute attacks terminate fatally the antecedent chronic and latent disease will be found to have been the real cause of death, if one looks a little below the surface. A curious feature of renal fibrosis, which is usually associated in the mind with the thought of contraction, is that the kidney may be of the natural size and even retain its ordinary weight and yet be exceedingly fibroid. If such a kidney be cut open it will be seen that the hilum is very much larger than natural and is filled with adipose tissue, while the renal substance which lies in a semicircle around it is reduced to such an extent that perhaps there is not more than one-half the normal amount of it. In this respect the kidney presents a parallel to a certain extent with what is so well known to occur in the liver in cases of hypertrophic cirrhosis. The difference, however, is that the fibroid liver may grow to be very much larger and heavier than natural, while the utmost that the kidney seems able to attain is to continue of normal size and weight when fibroid, instead of shrinking. It has been said that fibrosis is most apt to begin in the capsule and the subcapsular portions of the kidney. When the disease extends from this region it more frequently passes down the pyramids of Ferrein, which include the straight tubules of the cortex, than into the labyrinths.

Degeneration of the epithelium is more often seen in acute disease of the kidney than in the chronic forms, and when it is extensive in cases of slow disease like fibrosis it is the result of an acute process engrafted upon the chronic. The mode of its destruction varies very much: in some instances the lines of separation of cell from cell disappear, and the nuclei melt away, leaving nothing but an even granular mass of protoplasm, while in others the protoplasm is destroyed and the cell nuclei are left in so good a state of preservation that they are like the small cells which are so abundantly deposited in inflamed tissue.

No other organ produces a greater variety of disease of the blood-vessels than the kidney when it is fibroid. Illustrations of such vessels are included in the chapter on blood-vessels. Fibrosis of

the kidneys is so often found in persons who have died of pulmonary phthisis that there is no escape from the conviction that the processes are related, and this conviction is strengthened when it is recollected that the one essential of both diseases is the production of morbid fibroid tissue. There has been mentioned in this chapter an isolated growth which was found in the kidney in a case of Bright's disease which presented many of the physical characteristics of cancer, although nothing else of that nature was discovered at the post-mortem examination. In more than one instance it has happened to me to find in cases with malignant disease of the kidney that there were also lesions of Bright's disease which there was every reason to suppose had existed in the kidney before the malignant disease. Consideration of the life-history of cancer makes it appear that the theory of its extraneous and specific nature cannot be correct. It is not so well known by physicians as it should be that extensive fibrosis of the kidney may exist and yet the clinical evidences of disease be entirely wanting. The most striking features of the chronic diseases of the kidney which have been under consideration are that they are all so inextricably commingled that to attempt to separate them only causes confusion, and makes it evident that there is really only one disease, or that if there are subdivisions the differences are slight and the processes all related, and, further, that old age always brings fibrosis, and that when fibrosis comes early it is like age in youth.

CHAPTER XII.

THE SPINAL CORD.

The study of the pathology of the nervous system presents greater difficulties than that of the thoracic and abdominal organs, because of the great complexity of nervous diseases and the delicacy of the tissue. The results obtained from examination of the spinal cord are satisfactory because, owing to its cord-like form, a complete section across any part of it can be made and submitted to microscopical examination. Any disease, therefore, which traverses its length must be discovered if only a single section is thoroughly studied. This gives a certain completeness to sections of the cord. It must be confessed, however, that disease is more frequently found at different levels than extending through its length. The conditions in other organs are very different, and it is possible only to select minute pieces hap-hazard for microscopical examination or because some unnatural appearance has been observed with the unaided eye. Important disease for this reason often remains undiscovered. Most diseases of the spinal cord are to be recognized only by the use of the microscope, being undiscoverable by even the most careful examination with the unaided eye. There are few spinal diseases which produce such gross lesions as acute meningitis, in which sometimes a thick layer of yellow plastic lymph may be found within the dura mater entangled in the meshes of the pia-arachnoid. So serious a lesion as a complete transverse myelitis may exist and escape discovery at the post-mortem examination, to be demonstrated weeks afterward when the tissue has been prepared and sections have been cut for microscopical examination. Some years ago I published a report of a case of injury of the spinal column,* the result of an accident at sea, in which no evidence of disease was discovered at the post-mortem examination. Curious color changes indicative of lesions were evident after the tissue had been for some time in preservative fluid, and still later microscopical examination revealed the presence of a complete transverse myelitis

* A Study of the Paths of Secondary Degeneration in a Case of Injury of the Cervical Spine, by Arthur V. Meigs. American Journal of the Medical Sciences, August, 1890, and Transactions of the College of Physicians of Philadelphia, March 5, 1890.

and extensive disease throughout the cord. This fact, that extensive disease of the spinal cord may exist and yet escape detection unless searched for with the microscope, it is very important to keep constantly in mind, for it emphasizes the necessity for thorough examination of the cord in all cases, although there may be *a priori* no reason to suppose it to be diseased. In the chapters dealing with other organs it is pointed out that frequently, and especially in persons who have died of chronic disease, lesions are found of latent or chronic character that must have existed long before the attack that caused death. It will be shown as the subject of the pathology of the spine is developed that this is the case with it as much as with any of the other organs, and that therefore it is very desirable that the cord should be systematically and thoroughly examined in all the forms of chronic disease. This I have tried to do, but have succeeded to only a very limited extent, as a much greater amount of time could be profitably spent in the pursuit of such a study than the duration of any human life.

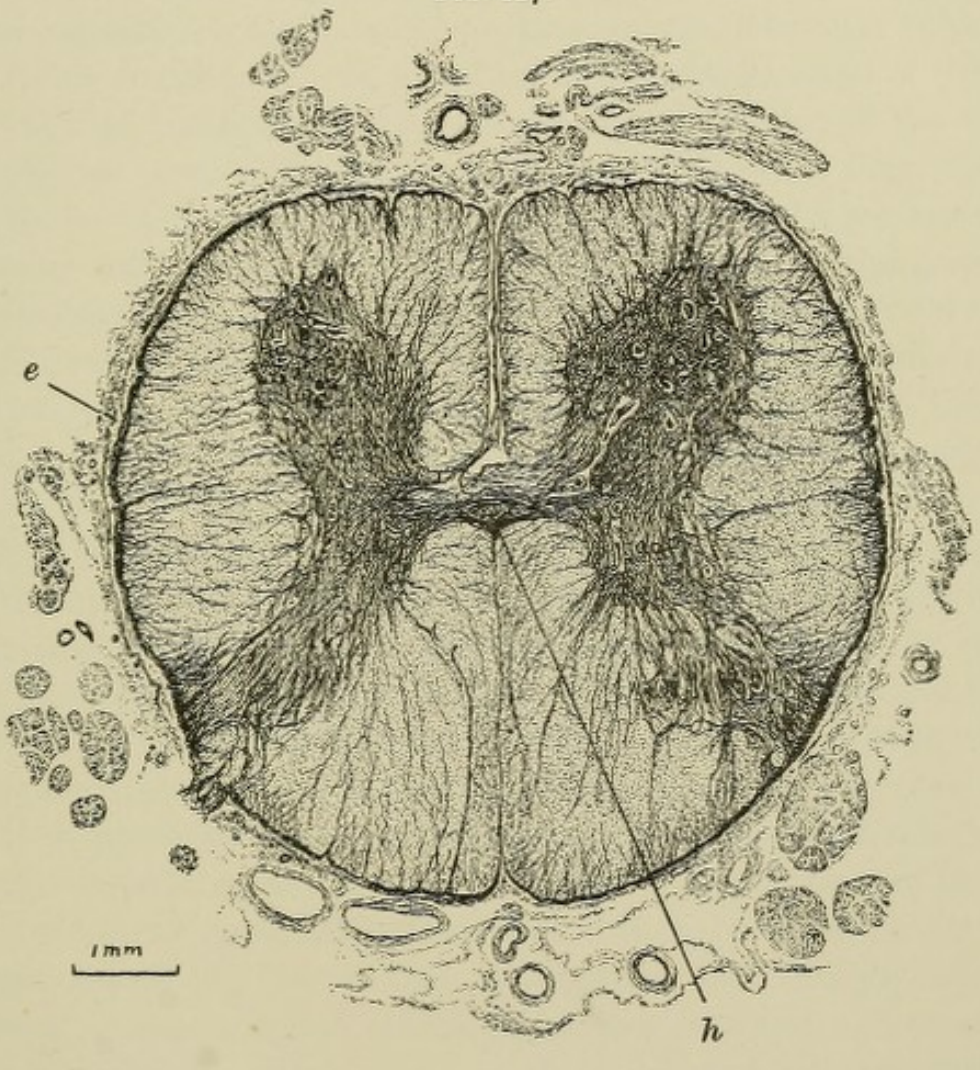
The greater number of spinal cords I have examined were taken from persons who died of diseases during the course of which there had been no clinical symptoms indicating involvement of the nervous system, and yet many of them show unmistakable pathological lesions. In the examination of nervous tissues it is necessary to exercise the utmost care in preserving and preparing them for microscopical study, so that changes due to faulty technique shall not be mistaken for disease. To accomplish this some uniform method must be pursued in all instances, in which case it will be known, after sufficient experience has been acquired to furnish a standard of ordinary conditions, that any unusual appearances must be the result either of disease or of post-mortem changes. In addition to a uniform method of examination as a basis, it is of course desirable to utilize other methods for the study of any disease discovered.

It is remarkable that in such chronic diseases as Bright's disease, and in others associated with it which involve the growth of great quantities of morbid fibrous tissue in the thoracic and abdominal organs, the same fibrous growth is found, if sought, in the spinal cord. This is true of cases in which there were not at any time symptoms pointing to disease of the nervous system. Fig. 127 represents the lumbar cord of a man fifty-seven years old who died of Bright's disease, with great fibrosis of the organs and extensive calcareous deposits in many organs and tissues and in the arteries, and without

FIG. 127.—PERIPHERAL FIBROSIS AND ENLARGED SOLID CENTRAL CANAL OF THE SPINAL CORD. (× 10.)

Lumbar cord from a man fifty-seven years old who died of Bright's disease. Around the periphery throughout almost the entire circuit the tissue is condensed and fibrous. The growth has been from without inward, and in the thickened portion the nerve elements have disappeared. At *e* the thickening reaches its maximum. The membranes are more closely adherent to the cord than is natural. The central canal (*h*) is much enlarged, is solid, and no epithelial cells can be seen in it. Figs. 128 and 129 are from the same case.

FIG. 127.



nervous symptoms. The drawing represents the commonest disease found under the circumstances. The lesions are not so obvious but that they might escape detection unless carefully sought. The membranes are more closely adherent than is natural around the entire cord, and the nervous tissue adjacent is condensed and fibrous. In these areas all trace of nerve elements has disappeared. The illustration exhibits a very slight degree of the change, and greater amplification is necessary to demonstrate minutiæ, but of the existence of the two features mentioned there can be no doubt. The central canal is larger than natural, is quite solid, and is composed of cells of very peculiar appearance, there being no trace of the columnar epithelium which forms so characteristic a feature of the central canal of the cord under natural conditions. The details of this disease of the central canal will be more fully discussed in connection with Figs. 136 and 137. So far as concerns the unnatural adhesion of the pia mater and thickening and fibrosis of the adjacent nervous tissue, the parallel is complete between such disease of the spinal cord and the fibrosis of the capsules and subjacent parts in the thoracic and abdominal viscera which has been said to be of such frequent occurrence. In this connection it may be mentioned once more that disease very commonly begins in the envelopes and at the surface of the organs. The cause for this, although at present hidden from us, should be diligently sought after, and will probably some day be found. It is likely that there is some connection between this special vulnerability to disease on the part of the surfaces of organs and their envelopes and the arterio-capillary fibrosis of Gull and Sutton. Although in their studies they confined themselves principally to the blood-vessels, they at the same time observed certain changes in the spinal cord which they minutely describe and illustrate.* There is every reason to think that they were to some extent incorrect in their conclusions regarding the condition of the fibrous coat of arterioles, and this probably was because the microscopical technique of that day had not been sufficiently perfected to enable them to study satisfactorily the finer histological conditions. On the other hand, to them is due the credit of having first demonstrated that Bright's disease is not a mere kidney disease, but that the growth of morbid fibrous tissue antedates the kidney lesions and is of greater importance, and that there are morbid lesions widely diffused through the body.

Fig. 128 is a section of the cervical cord from the same case as the

* Transactions of the Royal Medical and Chirurgical Society.

preceding. There is a large cyst with fibrous walls which lies in such a position as almost entirely to cut off the commissure. Fig. 129 is another picture of the cervical cord from the same case, and the section was cut less than an eighth of an inch away from the one represented by Fig. 128. In Fig. 129 also the cyst is included, but instead of interrupting the commissure it lies entirely behind it, in the white substance of the posterior columns, and its cavity is smaller and its walls are formed of much thicker fibrous tissue, from which strong prolongations extend in various directions into the nervous tissue around it. This cyst might by many be named a syringomyelia, but, whatever syringomyelias may be, and however they are caused, the cavity here shown presents in all respects the characteristics of cysts as they appear in other organs, and in this case there was also cystic disease of the kidneys. There is no reason to suppose that the cavity is anything but a cyst, and there is no known reason why cysts should not form in the spinal cord as well as in the substance of any of the other organs. Cysts are the result of a combination of morbid fibroid growth and degeneration of tissue, the existence of the two processes together appearing to be essential to their production. A cyst of such size as the one under consideration necessarily caused great destruction, and must have cut off a great many nerve fibres. It has been very generally accepted as a fact that such a destruction of nerve fibres causes degeneration of the cord for a considerable distance above and below the region destroyed. These secondary degenerations obey laws which are thought to be pretty well known, and they extend upward and downward in the cord along paths which have been determined by the observation of numerous cases of localized disease. In a paper already quoted* I have tried to show that this conclusion goes further than is warranted by the facts, and is not so accurate as is generally believed. Study of the cord in which the cyst was found confirms the views previously expressed, and perhaps does even more, for there is no secondary degeneration below the area of destruction by the cyst. Sections both of the dorsal and of the lumbar cord, prepared with great care and by more than one method, failed to show the slightest sign of any downward degeneration. Whether there was secondary degeneration extending upward in the cord from the cyst cannot be known, for none of the cord above the cervical portion which contained the cyst was retained for examination. This, however, makes no great difference, for, although it would have made the

* Page 155, *supra*.

FIG. 128.—CYSTIC DISEASE OF THE SPINAL CORD. (× 10.)

Cervical cord from the same case as Fig. 127. The cyst lies centrally in the cord. It is larger than in Fig. 129, has less thick fibrous walls, and occupies a different position, so that it almost entirely cuts off the commissure. The picture makes the cord appear a little smaller than Fig. 129 and of lighter color. This is owing to a different mode of preparation, which caused more shrinking of the tissue.

FIG. 129.—CYSTIC DISEASE, FIBROSIS, AND DEGENERATION OF THE SPINAL CORD. (× 10.)

Cervical cord from the same case as Fig. 128. The section here represented and that shown in Fig. 128 were not more than an eighth of an inch apart. The cyst lies in the white substance behind the commissure. Its cavity contained liquid and some solid structureless material; the enclosing walls are of dense fibrous tissue, and there are fibrous strands extending into the surrounding nervous tissue. The cyst would by many be described as a syringomyelia. *a* is a region in which the fibrous trabeculæ extending inward from the periphery and the fibrous elements generally are increased. It is shown more highly magnified by Fig. 132. *b*, an area of degeneration; better seen in Fig. 133, which is the same region more highly magnified.

FIG. 128.

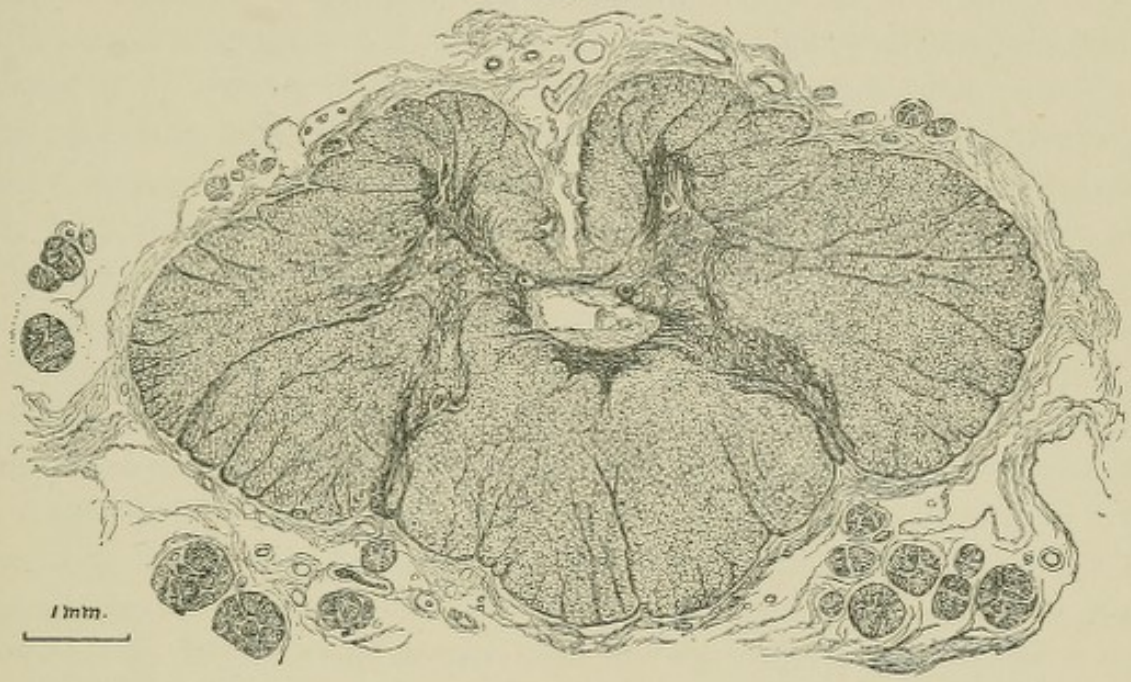
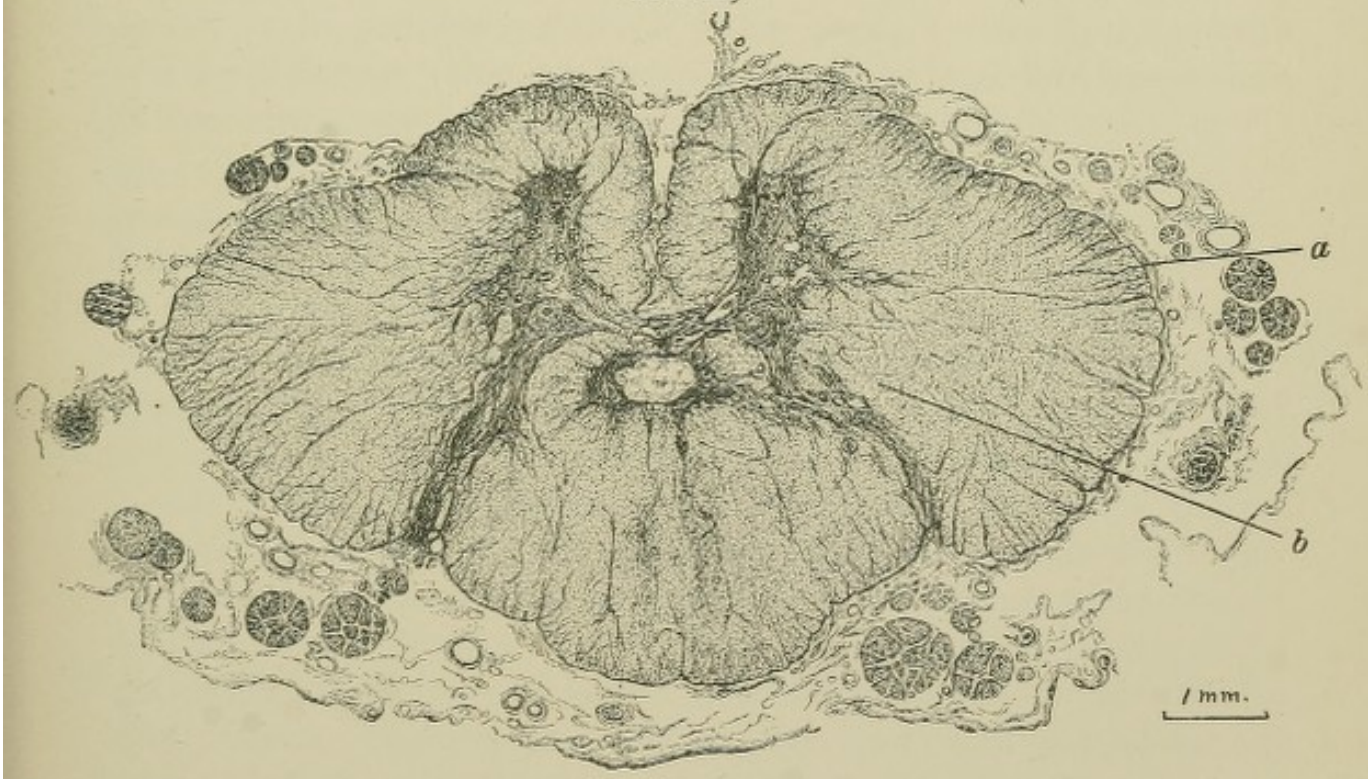


FIG. 129.



observation more complete to have found upward secondary degeneration absent, the proof is absolute that secondary degenerations upward and downward do not always follow as a consequence of local destructions, since it has been shown in a single case that there was no downward degeneration caused by such extensive local destruction as that occasioned by the cyst which has been described. The portion of cord illustrated by Fig. 129 shows other evidence of fibroid disease besides the curious and interesting lesions already described. It should be kept constantly in mind that the case was one of Bright's disease in which the kidneys were cystic and there was an extraordinary increase of fibrous tissue through the body, in the organs, and in the blood-vessels, with calcareous deposits to an unusual extent. In Fig. 129 it can be seen that the fibrous prolongations from the pia mater covering the surface of the cord are strong and heavy and extend as black lines deeply into the nervous tissue. It is a well-established anatomical fact that these extensions from the pia mater are natural, and that they constitute the fibrous framework which supports the delicate nerve tissue, and contain the blood-vessels which supply nutriment. The trabeculæ, however, in this cord are much thicker than is natural. In sharp contrast with the increase of density at the periphery, which is owing partly at least to the growth of morbid fibrous tissue, are the open structure and torn appearance of the central portion near the gray matter, especially in one of the antero-lateral columns. These two conditions, the dense and fibrous state at the periphery and the open nature of the tissue near the gray matter, are well shown so far as concerns their situation and general effects by Fig. 129, but to obtain an accurate comprehension of the changes which have been produced by the disease it is necessary to examine Figs. 132 and 133, which are more highly magnified views of portions of tissue representative of the two regions. Fig. 132, which is from the periphery, shows nerve fibres which are natural except that in a few of them there are slight indications of an early stage of degeneration; but the condition of the fibrous tissue is very different: the trabeculæ, two of which are included, are very much thickened and dense in structure. Even the fine fibrous strands that ramify among the individual nerve fibres have been tainted by the general fibroid growth and are less delicate than natural. Fig. 133, which represents a portion of the cord near the gray horn, is seen at a glance to present the greatest difference from the last-described picture. Instead of the nerve fibres filling almost the entire space, each

being a discrete whole, composed of an axis cylinder, white substance of Schwann, and encircling envelope, and closely surrounded by other similar nerves, the general effect is rather of confusion than of a well-ordered arrangement. There are scattered and broken shreds of fibrous tissue which form spaces of very various shapes and sizes. Some of these spaces appear empty, or there are axis cylinders which have not around them the natural cylinder of white substance and encircling envelope. Again, there are nerve fibres which appear natural except that their white substance of Schwann is muddy. The torn appearance of the tissue is striking, but besides this there is a decided increase of the amount of fibrous tissue, the strands being wider than natural, although less dense in structure than the trabeculæ in Fig. 132. The tearing apart must have been effected by some effusion such as occurs in the subcutaneous tissues in anasarca.

In considering the illustrations of spinal cord which have been thus far described, it must be remembered that all of them are from the same case, a man fifty-seven years old who died of Bright's disease but without having had any clinical symptoms to indicate disease of the nervous system. The lesions found were briefly as follows: adhesion of the pia with slight fibrosis of the adjacent nervous tissue, and a large cyst which had not caused any secondary downward degeneration, thus disproving the accepted doctrine that destructions of the cord always produce secondary degeneration above and below the primary lesion. Further, there was fibrosis of the peripheral region, the nerves remaining almost natural, while near the centre of the cord, besides the fibrosis, which was of different character from that at the periphery, the nerves were degenerated and the tissue torn by the action of some material which had been effused into it. The discovery of so many lesions of the nerves in a case from which all symptoms of nervous disease had been absent is very instructive when taken in connection with what has been so frequently said, that lesions may often be found if sought in organs in which there was no reason to suspect their existence from anything in the life-history of the patient.

Figs. 130 and 131 are from a man forty-two years of age who died of organic heart disease, a different condition therefore from the preceding case, but at the same time one closely allied to it, for the fact is well established that Bright's disease and chronic heart disease are intimately connected. The attempt has often been made to learn what the relation between the two diseases is, but nothing conclusive has been discovered; however, the establishment of the fact that there

FIG. 130.—DEGENERATION OF THE SPINAL CORD IN HEART DISEASE. (× 400.)

Section of the dorsal cord of a man of forty-two years who died of organic heart disease. The drawing is of a portion of the periphery, and includes pia mater (*p*) and adjacent tissue. All sharpness of outline has been destroyed. Only a few of the nerve fibres have distinct axis cylinders and clean white substance of Schwann; in most, the white substance has become muddy, the axis cylinders are ill defined, and the whole of the tissue is melting into a structureless granular mass.

FIG. 131.—DEGENERATION OF A PERIPHERAL NERVE IN HEART DISEASE. (× 400.)

From the same section as Fig. 130, a portion of one of the peripheral nerves. *n* is a large nerve fibre from which the axis cylinder has entirely disappeared and in which the white substance of Schwann is becoming muddy and granular. Many of the others are in a similar condition of destruction. In some fibres the white substance is even more granular than in *n* and the axis cylinders are gone, or again the white substance is very muddy but the axis cylinders remain. *f* denotes small nerve fibres which are very diseased. The small fibres in a natural condition are as distinct as the large ones, but nearly all those included in the drawing are so disintegrated that they appear as masses of densely granular material containing ill-defined circles. The extreme development of this disease is the conversion of nerve fibres into morbid fibrous tissue, as seen at such places as *b*, *b*. *h* indicates two small nerve fibres which still preserve all their distinctive characters but are in the first stage of degeneration, for their white substance of Schwann is muddy. The degeneration shown by the drawing is an advanced stage.

FIG. 132.—FIBROSIS OF THE SPINAL CORD IN BRIGHT'S DISEASE. (× 400.)

The region *a* of Fig. 129, more highly magnified. It is from the antero-lateral column at the periphery. *p*, pia mater, and *t*, *t*, fibrous trabeculæ extending from it inward. These fibrous columns and the pia are thick and heavy. The nerve substance itself is fairly healthy, the nerve fibres and axis cylinders being sharply outlined and the white substance of Schwann generally clean and white. In a few of the nerves the white substance is a little muddy. There is probably slight increase of the delicate fibrous strands among the individual nerve fibres. The nerves present a strong contrast with those of Fig. 133, which are greatly altered by disease.

FIG. 133.—DISINTEGRATION OF THE SPINAL CORD IN BRIGHT'S DISEASE. (× 400.)

The region *b* of Fig. 129, more highly magnified. A part of the antero-lateral column near the gray horn. The fibrous tissue is increased, but is of much less dense structure than that of Fig. 132. The outlines of the nerve fibres are ill defined, one not being sharply separated from another. In places the axis cylinders have disappeared and left large irregularly divided spaces which appear empty. The white substance of Schwann of many nerve fibres is muddy instead of pure white. The difference of the torn fibrous tissue of this region from the thickened and dense columns of Fig. 132 is very great.

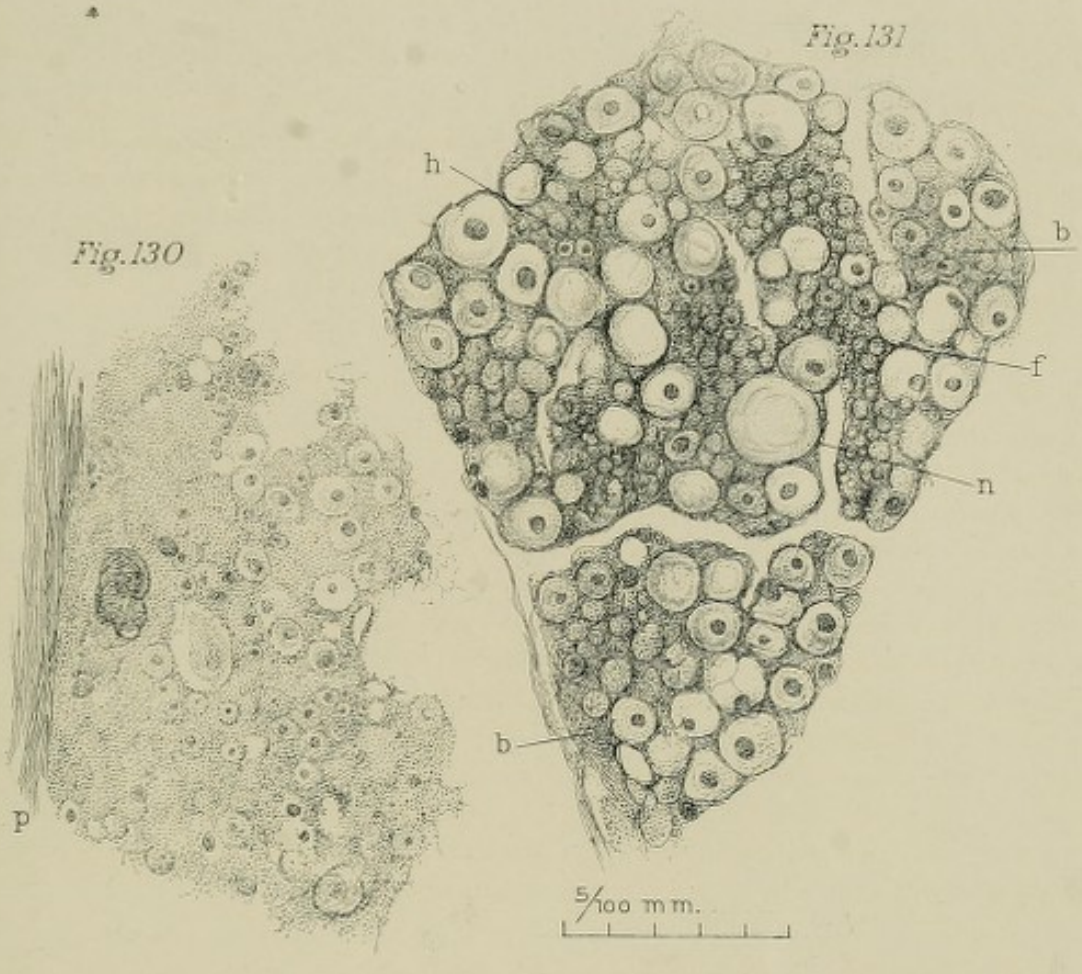


Fig. 131
h
b
f
n
b
Fig. 130
p
5/100 mm.

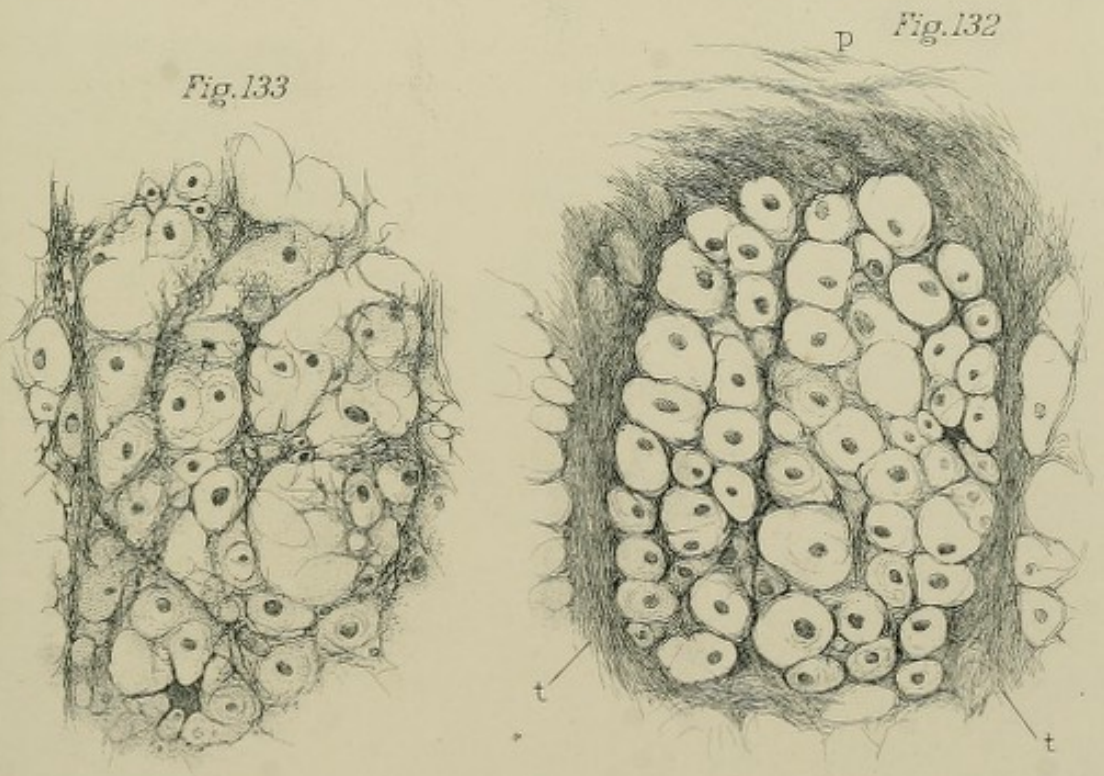


Fig. 132
p
Fig. 133
t
t

is a connection makes me believe there must be a common underlying cause which induces both of them. Fig. 130 exhibits a condition of disease which could not have been of very long standing, for the destruction of nerve fibres is so complete and extends over so great a surface that a considerable portion of the cord must have been rendered useless. There are hardly any nerve fibres which have distinct axis cylinders and clean white substance of Schwann. In most of them the white substance is muddy, the axis cylinders are ill defined, the external envelopes are indistinct or lost, and the whole of the tissue is melting into a structureless granular mass. A lesion like this was almost certainly developed during the latter part of the final illness, with the universal disturbance of the circulation and of the organs which occurs toward the end in persons dying of organic heart disease. Besides the disease which has been described, there were thickening of the pia, adhesion to the cord, and increase of the fibrous elements. Fig. 131 is a portion of a peripheral nerve which lay within the spinal canal, and it was included in the same section with Fig 130. The disease is as different as possible from that shown by Fig. 130, and must have been of much longer standing. There are chronic fibrosis and degeneration of the nerves. The larger nerves show a variety of changes due to disease, and hardly any of them can be said to be entirely natural. From many the axis cylinders have disappeared, and in such the white substance is muddy and of a yellowish color quite different from that of healthy fibres. In others the axis cylinders are enlarged, or their outlines are ill defined, or they have lost their solid look and appear as empty rings. The small fibres are perhaps even more greatly changed than the large ones. In healthy tissue the small nerve fibres are exactly like the large ones except in size, being composed of a distinct axis cylinder, white substance of Schwann, and sharply defined external enveloping ring. No such fibres are to be seen in the picture. There are a few in which the three component parts can all be distinguished, but even in these the white substance is muddy. Most of the small fibres have lost their distinctive characters and appear as confused masses of granular tissue containing rings, which are the remains of the external envelopes of the fibres. Various stages of this degeneration are to be seen, and it is evident that the process is one of fibrosis in which the nerve fibres themselves to a considerable extent are converted into morbid fibrous tissue. The nature of the lesions shown by this picture —fibrosis and this form of nerve degeneration—is such that it is cer-

tain they had existed for a considerable time before death, and yet, as in the first-mentioned case, there had been no symptoms of disease of the nervous system.

In the case which furnished the illustrations next to be described, a very different state of affairs obtained. The patient died at seventy years of age, having had for about ten years the symptoms of chronic degeneration of the spinal cord. His muscular power gradually diminished until he could neither walk nor stand alone, although there was no actual paralysis of any part. The muscles seemed stiff and hard, and when any movement was made it took him a long time to begin, and then it was executed very slowly. This delay to begin and slowness to execute movements after it has become evident that the person intends to perform some act requiring the use of the muscles are characteristic features of spinal degeneration, such as this man had. At the same time he grew very fat and his mind degenerated. There was no insanity, but he became irritable, his memory was impaired, and he was incompetent for any mental effort. During the course of the progressively increasing feebleness there was nothing to indicate other disease than that of the nervous system, except that the very first sign of a departure from perfect health was an attack of acute catarrhal pneumonia about ten years before he died. There never was any clinical evidence of disease of the kidneys, no albumen nor casts in the urine, nor any abnormal lowering of the specific gravity, and yet after death there was found fibrosis of the heart, lungs, liver, and spleen, and the kidneys were greatly contracted and their blood-vessels showed a great variety of disease. Fig. 134, which represents a section of the lumbar cord from the case of chronic myelitis just described, exhibits important lesions. The tissue, especially toward the periphery, is torn apart, so that it presents as open an appearance as a sieve, instead of being evenly solid as natural spinal cord is, and the central canal is enlarged and solid. The torn condition may be positively asserted to be the result of effusion into the tissue of the nature of dropsy. Of course the first thought that enters the mind of a pathologist upon seeing so singular an appearance as that represented by the drawing is that the effect was produced after death, owing to some fault in the preservation or mounting of the tissue for examination with the microscope, and that it is not disease, but post-mortem change. This was my own conclusion when spinal cord thus torn apart first came to my notice. The condition, which I have called dropsy of the spinal cord, is not rare in persons dead of

FIG. 134.—DROPSY, UNIVERSAL DEGENERATION, AND ENLARGED SOLID CENTRAL CANAL OF THE SPINAL CORD. (× 10.)

Section of the dorsal cord from a man seventy years old who died of chronic myelitis. The whole of the peripheral portion is torn and shredded out, while toward the centre it is less diseased. *g* is the central canal, which is much enlarged and quite solid. Figs. 136 and 137 are enlarged views of this central canal. Fig. 135 depicts more highly magnified a portion from the periphery and another portion near the centre of this same cord. *h* indicates a region where the tissue was slightly torn in preparation.

FIG. 135.—DEGENERATION OF THE WHITE SUBSTANCE OF THE SPINAL CORD. (× 220.)

From the same cord as Fig. 134, but another section differently stained. More highly magnified view. *a*, from periphery; *b*, from central portion. In *a* the tissue is torn apart and no nerve fibres of large size remain; while in the fibres still present the axis cylinders are enlarged and not sharply defined from the surrounding white substance of Schwann, which is muddy. There is fibrous increase, and an amylaceous body is included. *b*, from the central portion, is less diseased. The axis cylinders of the large nerves are small, ill outlined, and some of them eccentrically placed. The smaller fibres are not sharply outlined, and the white substance of Schwann is muddy. Many nerve fibres have disappeared, and are replaced by the dark material, which is morbid fibrous tissue. The most striking contrast, perhaps, is that *a* is broken and has torn and scattered shreds of nerves, while *b* is a solid tissue.

FIG. 134.

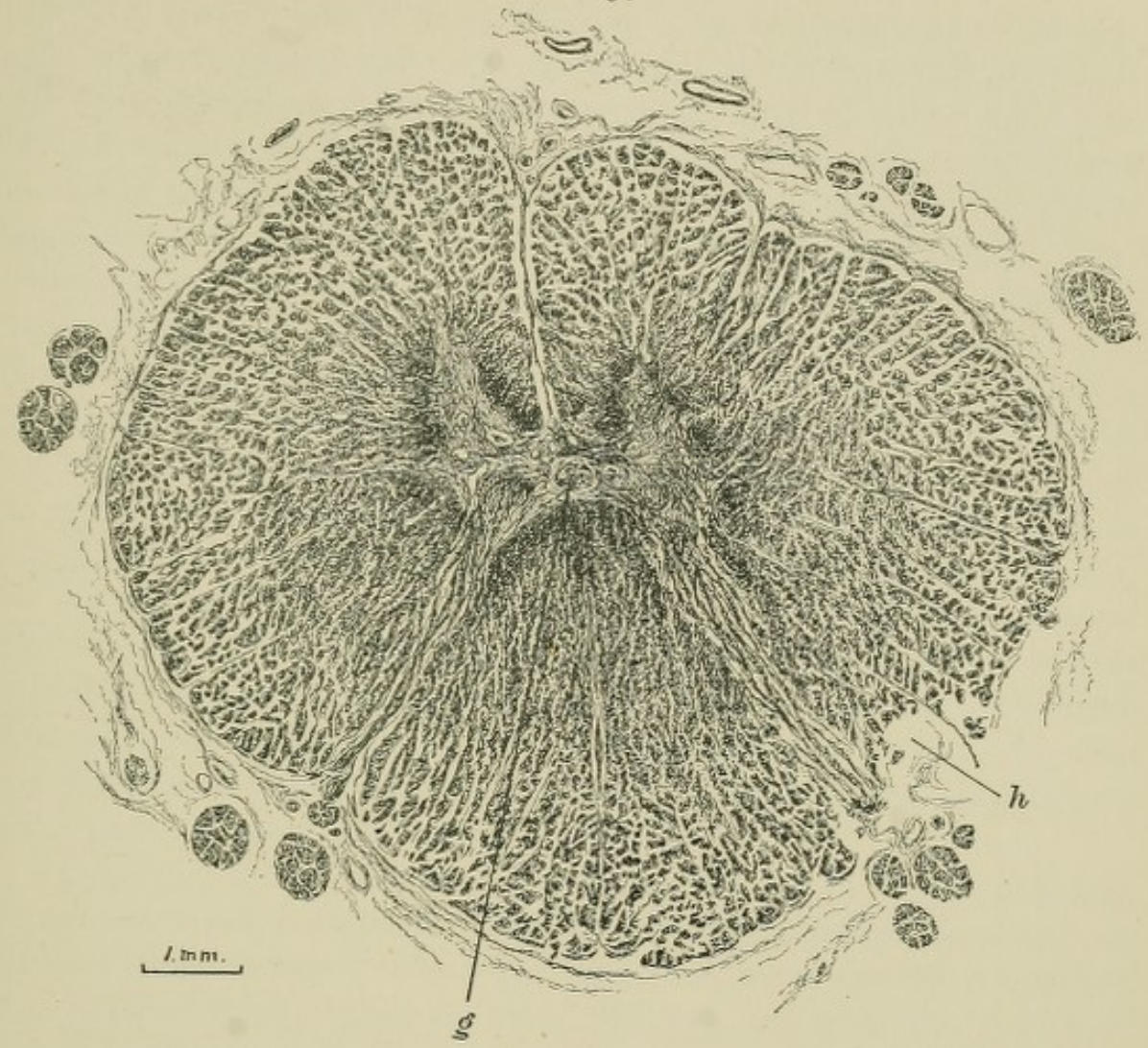
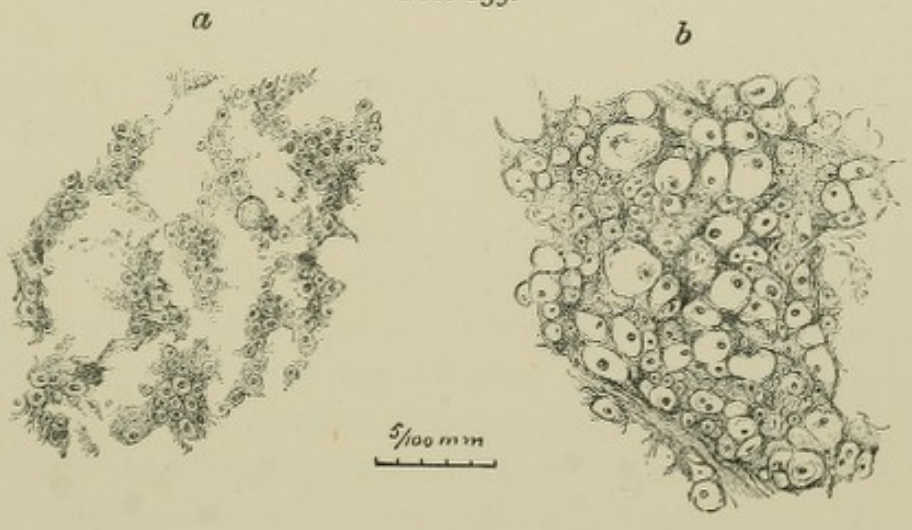


FIG. 135.



chronic disease, even if there were no clinical symptoms of nervous disease during life. For some time after first seeing the lesion I supposed it was caused by fault in my technique, but at last I was shaken in this opinion by finding in one of my cases that, although different pieces of the tissue were prepared and mounted in various ways, the appearance of the dropsy was equally distinct in all of them. After having found this sufficiently often it was impossible to continue to believe it a post-mortem change or due to bad technique, and I was driven to the conclusion that it must be a state of disease. There is no reason why effusion producing a condition of dropsy should not occur as well in the spinal cord as elsewhere, especially as the cases in which the lesion is most frequently found are those chronic ones in which transudation into the cavities, tissues, and organs is common. In the case under consideration four sets of sections of the cord were prepared separately, two by a skilled microscopist and two by myself, and in all of them the cord-tissue had the same sieve-like appearance. Consideration of the reasons that have been detailed warrants the conclusion that the lesion is the result of transudation and constitutes a true dropsy of the spinal cord.

In addition to the dropsy, which is so well shown by the drawing, the tissue is degenerated, but this can hardly be distinguished without greater amplification. Fig. 135 represents, more highly magnified, two portions of the tissue shown in Fig. 134, one from the periphery and the other from the centre near the gray horn. The drawing of the peripheral region (*a*) makes very evident the dropsy; the tissue is so torn apart as to give the impression of a great amount of empty space, the amount of this apparently empty space which was filled by the transuded material exceeding that occupied by solid tissue. The solid tissue is all greatly degenerated. The axis cylinders are enlarged and their outlines are not sharply defined from the surrounding white substance of Schwann, which is muddy instead of being entirely unstained as is the case in healthy fibres. Morbid fibrous tissue lies among the fibres, having grown at the expense of the nerves, and one of the bodies which have been named corpora amylacea is included. They are produced only by degeneration. Such an effect must have been produced in the course of a long period by the gradual growth of fibrous tissue and degeneration of the nervous elements, and, finally, not long before death came the dropsical transudation which tore open the tissue and completed the work of destruction.

The tissue from the centre near the gray matter (*b*, Fig. 135) pre-

sents the strongest contrast to that from the periphery. It is quite solid and firmly knit, and yet shows evidence of disease as unmistakable as the torn tissue. The most striking and certainly the most important feature is the increase of fibrous tissue. The strands running among the nerve fibres are heavy, but still more striking is the conversion of the smaller nerves into morbid fibrous tissue. None of the small fibres are natural in appearance. They are dark-colored, and the outlines of their component parts are indistinct. In none of them is the white substance unstained and white as in healthy nerves, and the axis cylinders and external envelopes of the fibres are in all stages of indistinctness. In natural cord almost all the space between the large fibres is filled by small ones whose characteristics are as distinct as those of larger size. In the picture the space between the large fibres is occupied by morbid fibrous tissue which was formed out of destroyed nerve fibres and by other fibres which are in all stages of degeneration, and which were evidently in process of destruction and would have been converted into fibrous tissue had life been sufficiently prolonged. The large fibres also are diseased, although much less so than the small ones. Their axis cylinders are eccentrically placed, are rather small, and have not the sharpness of outline of healthy nerve fibres. No part of the tissue, therefore, was in a natural condition.

It was mentioned in connection with Fig. 134 that the central canal of the cord is enlarged and solid, but the structure and peculiarities were not described. Fig. 136 is this central canal more magnified, and it shows a curious condition of disease. It is well known that the central canal changes as life advances, and the following expresses the accepted views of histologists upon the subject: "The cords of children and of many animals contain a completely pervious central canal; in the human cord in later life this is usually more or less occluded, although much variation exists in this respect. The upper cervical, lower lumbar, and sacral regions usually contain, even in the adult, a partially pervious tube. Overgrowth of the lining cells, as well as the subepithelial substantia gelatinosa, is the principal factor in the closure of the central canal, which, however, must be regarded as a normal change and not a pathological process."* The changes which take place in the tissues between birth and old age are highly interesting, and it is quite true within certain limits to say that those described as occurring in the central canal must be regarded as normal and not as

* Normal Histology, by George A. Piersol, Philadelphia, 1893.

FIG. 136.—ENLARGED SOLID CENTRAL CANAL CONTAINING A BLOOD-VESSEL. (× 50.)

Section of the lumbar cord from the same case as Fig. 134. *a* denotes the anterior and *b* the posterior aspect. *c* and *d* are the two lateral boundaries of the central canal, which is very large, completely solid, and shows no trace of epithelial cells. Its anterior and posterior boundaries are easy to distinguish in the drawing. *e* is a blood-vessel. Fig. 137 is an enlarged view of the blood-vessel (*e*) and surrounding material.

FIG. 137.—BLOOD-VESSEL IN THE ENLARGED SOLID CENTRAL CANAL OF THE SPINAL CORD. (× 220.)

Enlarged view of the vessel *e* in Fig. 136 and of the surrounding cells. The vessel contains many red and white blood-corpuscles and in structure is like a capillary. The cells by which it is surrounded are of unusual appearance and cannot be satisfactorily classified. They are not epithelial, nor are they like leucocytes. It is evident that the material which filled the central canal and enlarged and made it solid was a living growing tissue with a blood-supply, but its cellular composition is not like that of any of the ordinary tissues.

FIG. 136.

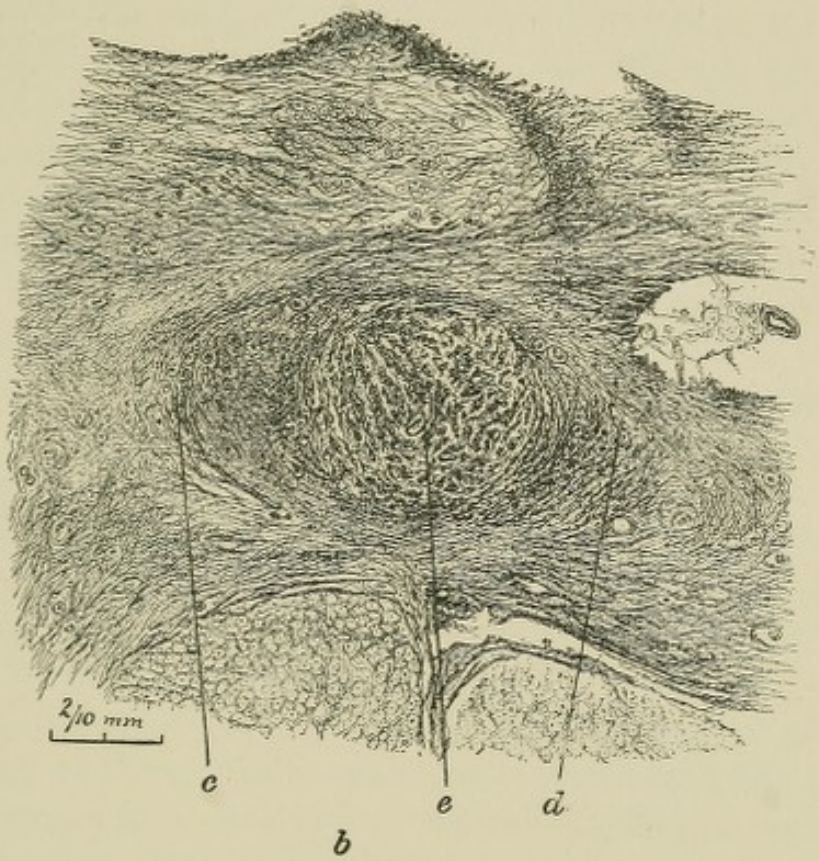


FIG. 137.

pathological processes. On the other hand, it is equally true that it is very common for such changes to become so exaggerated that they must be looked upon as pathological. The difficulty of the question is reached when the attempt is made to decide in an individual case whether conditions found are to be classified as belonging to the normal changes or are pathological. Fig. 136 exhibits a peculiarity which settles any question that might be raised as to whether the tissue is diseased: there is a blood-vessel in the very centre of the solid tissue which was once the canal. The vessel was found to be present in a number of sections of this portion of the cord. No one has ever pretended to say that blood-vessels like this exist in the normal central canal of the cord, which is the remnant of the neural tube of the embryological period. This blood-vessel is in structure like the normal capillaries. It belongs to the class of vessels which are prone to develop in new tissues or in tissues which, owing to hypertrophy, outgrow their ordinary vascular supply. Besides the positive evidence of disease afforded by the presence of a blood-vessel in the normally avascular central canal, the nature of its tissue, its size, and its relations to the surrounding nervous tissue are such as to render it impossible to consider it a normal condition. The description quoted shows that closure of the canal is a common occurrence. The lining cells are well known to be columnar epithelium, and in the young human subject and even in elderly persons their columnar character is often easy to recognize. The histological description is that the cells of the canal undergo proliferation until the central space is closed, but it is not asserted that it ever becomes greatly enlarged and its cellular formation entirely changed. In the drawing nothing resembling in the slightest degree the natural epithelium can be seen, and the canal is at least two or three times larger than natural. Its boundaries are shown by the drawing, and, besides the great enlargement, it is seen to have grown in such a way as to imitate the appearances produced by a neoplastic tumor growing in one of the organs. At its periphery the tissue is arranged in curving lines, and at the junction of the diseased tissue with the surrounding nerve substance the two merge together in such a way that it is hard to say exactly where one ends and the other begins. Some such effect is always produced when growth takes place from a central point so rapidly that the surrounding parts are destroyed or squeezed aside to make room for a new and enlarging tissue. The imitation of tumor growth with crushing and destruction of the surrounding nervous

material could hardly be more striking than it is, and it is impossible that such growth should have occurred without injury to the cord. Fig. 137 is an enlarged view of the blood-vessel and surrounding tissue from Fig. 136, and shows that it is structurally like a capillary and contains both red and white corpuscles and is surrounded by a lymph-space. In all these particulars its characteristics are the same as those of new blood-vessels, which have already been described as they develop in new or hypertrophied tissues (Chapter IV.). The tissue by which the vessel is surrounded is difficult to describe. It is not like epithelium, connective tissue, or any of the normal gland-cells, but is evidently a cellular structure of aberrant type, and therefore should be classed with the tumor growths. Before finally leaving the consideration of this curious case of chronic myelitis, which proved also to be one of Bright's disease, it may be well to pass in review the lesions which were found as the result of careful microscopical examination of sections of the cervical, dorsal, and lumbar portions of the spinal cord. (1) The tissue was torn apart and split open so as to present an almost sieve-like appearance; this has been said to be a form of dropsy. (2) Near the periphery there was extensive fibrosis and the pia mater was adherent to a greater degree than natural. (3) The central canal was solid and enlarged, the columnar epithelial cells had entirely disappeared, and new vessels had developed in the proliferated tissue. (4) Throughout the cord there was general fibrosis, and the nerves were greatly degenerated and many of them destroyed. The impression was that the actual number of nerves was less than in healthy nerve-tissue. The changes were most extensive in the posterior columns. (5) There were many corpora amylacea, and the Deiters spider-cells seemed too numerous and prominent. (6) The multipolar ganglion-cells gave the impression of being less numerous than usual, and appeared shrunken and ill preserved. (7) The peripheral nerves included with the sections of the cord were fibroid.

Throughout what has been written of the thoracic and abdominal organs and lastly of the spinal cord the fact has been repeatedly dwelt upon that pathological lesions are often found, if sought, in other organs than those in which they might, from the life-history, have been expected, such lesions having occasioned no clinical symptoms to direct attention to organs greatly diseased. Ordinarily in cases of chronic disease many of the viscera, and occasionally all of them, are involved. To a certain extent the lesions found in different organs are similar, although the clinical manifestations are infinitely

various, sometimes one and sometimes another of them being the victim upon which the disease falls. The similarity consists in this: no matter how much the lesions may vary in other respects, increase of fibrous tissue and vascular disease are common to them all.

All the illustrations of the spinal cord which have been described were furnished by three cases, and they afford an interesting confirmation of the fact that, with lesions somewhat parallel and of wide-spread extent, the clinical manifestations were as different as it was possible for them to be, and there was no evidence in regard to how many and which of the organs were diseased. The first case was one of Bright's disease with extensive organic disease of the thoracic and abdominal viscera, but no symptoms of nervous disease, and yet the lesions of the spinal cord were of so gross a character that it was wonderful how they could have existed without external manifestation of their presence. The second case was one of disease of the heart, and was like the first in the relation of symptoms to lesions. With organic disease of the heart and of other organs and the ordinary clinical symptoms manifest, there was nothing in the life-history to indicate involvement of the nervous system, and yet the lesions of the cord, although less coarse, were as unmistakable as those found in the first case. In the third case the conditions were exactly reversed: from the beginning it was evidently one of disease of the nervous system, and there were never any symptoms indicating involvement of the thoracic and abdominal organs. Although disease of the kidneys was always suspected, no evidence of its existence during life could at any time be obtained. The autopsy demonstrated that, besides the destructive lesions of the spinal cord, contracted kidney and fibroid disease of other organs existed.

No three cases could more strikingly demonstrate the existence of lesions in other organs than those in which they might have been expected from a routine interpretation of the clinical symptoms. The three cases illustrate also the wide-spread extent of organic lesions in chronic disease. Although so instructive if properly appreciated, the symptoms and disease which have been described are all of every-day occurrence.

Besides what has been detailed of disease of the spinal cord, many curious things have come to my attention in the course of the examination of cords taken from cases of various diseases. In typhoid fever, for instance, the cord is never healthy. The appearances are not easy to describe, and are perhaps even more difficult to interpret,

because in diseases like typhoid fever, in which the blood is greatly disorganized, the tissues are always in a condition which renders them unsatisfactory for microscopical examination. The cells do not differentiate sharply, and all the tissues are clouded and obscure. It is not possible that this is entirely due to post-mortem change, for it is found to a greater or less extent in all cases. It must be partly at least the result of disorganization which occurred during life. The condition and appearance of patients in the last stages of typhoid fever are more like those of dead than of living persons, and this suggests that there may be death of the tissues while the life of the individual still continues. Making due allowance for this fact of a general disorganization of tissue in typhoid fever, the cord often presents lesions which are the results of disease and could not have been produced post mortem. In such cases of typhoid fever as I have examined after death, the cord has given the impression that it had been affected by inflammation. The axis cylinders of the nerves in the cord, and still more those of the peripheral nerves, are swollen. The fibrous envelopes of the cord also appear to be unnaturally adherent and perhaps a little thickened. These changes of the cord in typhoid fever are of such delicate nature that it is difficult to be certain of their existence, but there cannot be any doubt that they constitute positive disease. The subject was discussed by me in a paper published some years ago.*

In brain syphilis the cord was found to be fibroid at its periphery, in the same manner as it has been said is sometimes found in Bright's disease, and in a case of malignant disease of the abdominal viscera, besides bony plates in the pia-arachnoid, this same thickening and fibrosis of the peripheral portion of the spinal cord were found. It seems likely that the fibrosis in this latter case had antedated the malignant disease, for fibroid material is usually slowly developed. It is impossible to say that fibrosis had no influence in inducing the malignant disease. Certain it is that the tissues of older persons are much more prone to malignant disease than those of the young, and fibrosis is in its nature a disease of age. Bony plates, as they are called, are so commonly present in the membranes of the spinal cord that Wilks and Moxon † say that "half the population at thirty-five have a few," and,

* The Morbid Anatomy of Typhoid Fever. The Annual Address, delivered before the Philadelphia Pathological Society, by Arthur V. Meigs. Medical News, November 15, 1890.

† Pathological Anatomy, second edition, Philadelphia, p. 247.

further, that "it is a great and rather common proof of ignorance of the spinal cord to treat them in a post-mortem examination as if they bore on the symptoms of the case." Although it is true that they have no discoverable influence in producing symptoms and are exceedingly common, it is important to keep it in mind that they must be looked upon under all conditions as the result of a disease process. Their presence is an evidence that the fibrosis which is inevitable to the advance of years has begun in the individual in whom they are found, and that therefore his bodily condition, which at one time was more nearly perfect, has somewhat deteriorated.

In the case of a young man who had had pulmonary hemorrhage and died with the symptoms of acute meningitis, besides a large cavity in one lung and other lesions of tuberculosis, the condition of the spinal cord was interesting. There was nothing like miliary tuberculosis, nor anything else to show that the meningitis was tubercular, although the lesions in the lung were typical. The disease of the meninges was distinct, there being extensive infiltration especially of the vessels and along the extensions of the pia mater which penetrate the substance of the cord. Besides this condition of the membranes, however, the cord itself was greatly involved, there being much destruction of the nervous tissue. In places the axis cylinders were swollen and in other places had disappeared entirely; this degeneration was most extensive in the posterior columns. It is instructive to note that this disease of the cord presents a precise parallel to what has been described as so common in chronic diseases involving the thoracic and abdominal viscera, as there is extensive disease of the coverings—meningitis—and at the same time great degeneration of the organ itself, in this instance the cord. The question cannot be answered whether the meningitis, which was the direct cause of death in a man who had also pulmonary tuberculosis, is to be looked upon as a part of the tubercular process or was an accidental intercurrent attack of different nature. If only tuberculosis was regarded as the result of tissue-change, due to a misdirected growth and to degeneration in which the process of inflammation plays the most important part, it would be much less difficult to comprehend the combination in the same individual of pulmonary phthisis and acute meningitis. Previous to the introduction of the germ theory of disease, which necessitates the belief in the influence of an infection from without in all cases of tuberculosis, it would not have seemed unreasonable to suppose that both the pulmonary disease and the disease of

the cord had had a common origin in some tendency which as yet defies our understanding. This would not seem more extraordinary ignorance than our ignorance of the reason why the tubercle bacillus grows luxuriantly in the lung of one man and utterly fails to grow in another.

In all the diseased spinal cords examined by me the peripheral nerves, portions of which are always included with sections of the cord, were found to have participated in the morbid process. The blood-vessels also are commonly involved, often being thickened in much the same way as in the other organs. The vessels of the cord, however, differ somewhat from those of other organs, being more delicate, and those which lie in the membranes around the cord present the further difference that they are unsupported. In most tissues and organs the vessels are tubes which are closely surrounded by a solid medium, whereas the arachnoid and pia mater are loose-meshed and serve only to hold the vascular tubes in position, giving no support to their walls. These anatomical conditions make the vessels of the cord different from those of other organs, and they seem to me less liable to disease, especially to great thickening of their walls, which has already been shown to be so very common in the blood-vessels of the thoracic and abdominal viscera.

At present meningitis is looked upon as common, and the diagnosis is frequently made by physicians who recognize several forms of the disease. On the other hand, from the clinical stand-point myelitis is considered to be rare. In none of the cases of meningitis that I have studied with the microscope have the lesions been confined to the membranes and exterior of the cord, but in each instance there has been evidence of inflammation of the cord itself, some of the axis cylinders being swollen and others destroyed, and parts of the tissue becoming unusually red when stained with carmine, as is generally the case in inflammation. This view having been confirmed by the pathological evidence, it has become little short of a certainty. This recalls what has been so often mentioned in the preceding chapters, the strange way in which the envelopes of all the great organs of the body become inflamed and thickened and adherent to surrounding parts. This sometimes occurs when the organs themselves are greatly diseased, and is only a part of the general process, and at times it happens when the organs seem healthy. The precise meaning of all this is not understood, but the observation makes it certain that the surfaces of the organs and their

envelopes are the most vulnerable parts of them, and are much more liable to disease than the deeper portions.

Those in charge of institutions for the care of the insane have been reproached with having done little or nothing to advance our understanding of pathology. So little was known of the pathology of insanity that it has even been said that the nervous tissues do not undergo physical change in true insanity. Recently, however, there have come from alienists a number of instructive essays directing attention to lesions of the nervous system and to their connection with lesions of the thoracic and abdominal organs. They have pointed out that Bright's disease and pulmonary phthisis and all the chronic bodily diseases are often connected with mental unsoundness, and that lesions of the nervous system, which it is now well known frequently exist, are often connected with extensive bodily disease.

Before dismissing the subject of the nervous system a few words must be added concerning the brain. Less advancement has been made in the pathology of the brain than in that of any of the other organs. As has already been said, its anatomy is so complex and it is so delicate as to be more difficult to examine satisfactorily than any other tissue. The grosser forms of disease to which it is subject, such as tumors and extensive degenerations, have long been known, and recently great advances have been made in our understanding of its anatomy and physiology. The difficulty, however, that confronts the pathologist is, in the first place, that if there is no lesion sufficiently gross to be discoverable by the unaided eye microscopical study is almost hopeless. The size of the brain is so great that it is impossible to examine into the structural condition of the whole of it with the microscope, and therefore all that can be done is to study portions of it taken hap-hazard. In such an examination it might well happen that the portion studied would prove perfectly healthy while if the section had been taken from another region close by extensive disease would have been found. Besides this, it must be confessed that our comprehension of the minute anatomy and physiology of the brain is still so imperfect, and the best methods of microscopical technique for its examination still leave so much to be desired, that often it is impossible to be certain whether minute changes are the results of disease or are due to faulty preservation or preparation of the specimen. My own studies of brain tissue might have been more extensive, but they have led to one or two observations which are worthy of mention. In the case of death from meningitis of a man

suffering with pulmonary tuberculosis, mentioned in connection with the discussion of the spinal cord, it was found that there was cerebral as well as spinal meningitis. Study of the brain with the microscope showed that just as there was myelitis in connection with the spinal meningitis, so there was cerebritis wherever the cerebral meninges were inflamed. This raises again all the questions parallel to those which were discussed in connection with the relations of spinal meningitis and myelitis.

In studying a case of brain syphilis, I was somewhat surprised to find that in the diseased areas the blood-vessels were little if at all involved, and that the disease consisted in the replacement of the ordinary brain tissue by morbid fibrous tissue. The blood-vessels of the brain are well known to be as subject to disease as those of any other organ. The disastrous consequences of rupture of the cerebral vessels, which causes paralysis, are so well known as hardly to require mention. It is my opinion that in apoplexy ulceration of the blood-vessels is most commonly the precedent disease. This causes slowly increasing thinning of the arterial wall until perforation takes place without strain or violence. Apoplexy is not usually due to the rupture of a stiffened and weak vessel caused by muscular effort, nor does it commonly occur because the heart has for some reason driven the blood onward with unusual force. In most cases neither violence nor effort has any influence in causing the final rupture of the artery, for generally apoplexy comes on while the individual is sitting quietly or even lying down. The process is one of ulceration exactly similar to perforation of the intestine in typhoid fever when the rupture takes place as the patient lies quietly in bed. In several cases of cerebral apoplexy which have come under my notice the blood-vessels were found ulcerated and thinned, and in one the vessel at the seat of hemorrhage was found in this condition of ulceration, with the opening in it still visible. The blood-vessels of the brain are liable to thickening of their coats in a manner similar to that which is so common in the other organs. This I described in an illustrated essay published some years ago.*

* A Study of the Arteries and Veins in Bright's Disease, by Arthur V. Meigs. Transactions of the College of Physicians of Philadelphia, June 6, 1888, and Medical Record, July 7, 1888.

CHAPTER XIII.

DIAGNOSIS IN CHRONIC DISEASE.

It is not intended here to enter upon a discussion of the diagnosis of such diseases as are well understood and have, therefore, been satisfactorily classified, but to deal with those which have been under consideration in the preceding pages. It has been indicated that many of the commonest diseases, if not most of them, are little understood and are therefore ill classified, and that for these reasons their diagnosis is very difficult. Heretofore diagnosis has been narrowed by the prevalent conception that disease usually lights upon one organ or another and confines itself to a restricted district. In the endeavor to combat this error it has been repeated so often as perhaps to make it a wearisome reiteration that disease is generally widespread in its effects, and that latent and chronic disease has an almost inconceivably great influence in starting attacks that appear purely acute and in determining their course and outcome. The diagnosis of chronic disease, and the relations of diseases not usually supposed to be connected, are the subjects which I desire to discuss, and with these will be included such observations as it has been possible to make which seem to show that any of the ordinarily accepted doctrines are founded on error.

From the study of what has been named Bright's disease more has been learned in the direction indicated than from any other source. It is impossible to bestow close attention upon this curious condition without noticing that at one time or another it has been made to include symptoms indicating disease of every organ of the body, and if the subject is pursued to the post-mortem room the fact is forced upon the attention that every part of the organism is liable to become the subject of lesion. Cases usually classed as chronic organic heart disease, and occasionally those of chronic disease of the brain and spinal cord, also illustrate the fact that the lesions in organic disease are widely spread through the body. No better method of elucidating the degree of accuracy and at the same time the limitations of diagnosis as ordinarily pursued could be obtained than from a consideration of a suitable illustrative case. In this way may be shown what

disease was thought to exist during life, and the post-mortem examination can be used to verify the results, showing how accurate the diagnosis was, in what it failed, and what must be done to attain greater exactitude in the future. The case which will be narrated was one which seemed to be of commonplace nature, and nothing but the very careful and thorough study post mortem made it so interesting and instructive. In the hospital in which the man died the case is recorded as one of Bright's disease. A number of the illustrations which have been included with the discussion of disease of different organs were taken from this case.*

A man of fifty-seven years, who had had various attacks of illness during his life and had been dissipated but had as a general thing enjoyed good health, noticed that he was very short of breath on going up-stairs. This was about six months before his death, and was the first warning he had of any departure from his usual good health. Soon afterward he "took cold," his feet swelled, there was difficulty of breathing, and he became very weak. He often had pain in the region of the heart, but had no cough or urinary or bowel disturbance. In the hospital it was found that the urine contained a small amount of albumen and hyaline casts. The radial and femoral arteries were stiff, and there was more visible pulsation of the arteries near the surface than is usual in healthy persons. The cardiac impulse was diffuse, but not of great force. At the apex of the heart both sounds were distinct, and there was a systolic murmur. In both the pulmonary and the aortic region a systolic murmur was audible. At the bases of the lungs posteriorly there was great impairment of the percussion resonance, amounting almost to dulness, and greater on one side than on the other. There was almost entire absence of breath-sounds at the bases, more positive on the side which was dull on percussion. At the middle portions of the lungs there were some crackles, and at the apices the sounds were natural. At places over the posterior portions of the lungs percussion caused pain. There was no increase of the area of percussion dulness over the liver, and in the region of the usual splenic dulness there was tympany. The abdomen was somewhat full, and there was fluctuation. The patient's intelligence continued good, but the dropsy and orthopnœa increased, and he became extremely restless and distressed. There were constant pain and breathlessness, to such a degree that he

* Figs. 7, 28, 29, 36, 48, 49, 50, 67, 85, 89, 109, 127, 128, 129, 132, and 133 were all from this case.

was in torture, which continued until his death. There are few diseases in which death is more painful than in Bright's disease when the final illness is greatly prolonged. The post-mortem examination showed the heart to be about one and a half times the natural size, and the tissue exceedingly hard and tough. Upon the inner surface of the ventricles there were whitish fibrous spots which upon section were seen to be about one-sixteenth of an inch thick. The mitral valve was somewhat thickened and its cords shortened, allowing less free motion than natural. The aortic valve-flaps contained small deposits of chalk which somewhat stiffened them. The aorta was natural to the diaphragm, but the abdominal aorta and the iliacs were very atheromatous and chalky. The vena cava and iliac veins looked natural. The lungs were everywhere firmly adherent. On section they appeared intensely congested and in places were nearly solid. Such portions of the lungs were very dark-colored. The pleura was greatly thickened. The abdominal cavity contained a large amount of fluid. The liver was rather small, and weighed two pounds and six ounces. It was firm in texture, and on section the fibrous tissue seemed increased in quantity. The spleen was of normal size, but very hard, and its capsule exceedingly thick. The walls of its arteries were so much infiltrated with chalk that they were stiff like bony tubes. The intestines appeared to be normal, except that the calibre was small from contraction and the gut seemed to be unusually short. The mesentery and greater and lesser omentum were much infiltrated with chalky masses, so that they were snarled and twisted out of shape. In the posterior walls of the abdominal cavity there were large and extensive chalky deposits. The kidneys were small, firm, and dark-red in color, and the capsules thick. They weighed together nine ounces, and appeared to be not more than two-thirds the natural size. There was positive but not very great increase of the subarachnoid fluid. The carotid and vertebral arteries at their entrance and for half an inch within the skull were thick and white. The vessels of the dura mater looked thick. The brain-substance appeared normal. The spinal cord looked natural, but there were a few bony plates in the posterior portion of the pia-arachnoid in the dorsal region. There were numerous ecchymoses of the skin of the posterior part of the body. Many sections of various organs and tissues were cut and examined with the microscope, and they demonstrate an extraordinary condition of disease, when it is recollected that the case was one of ordinary Bright's disease. In connection with the illustrations the

various lesions are discussed in their appropriate places. The microscopical examination demonstrated extensive disease of the blood-vessels, disease of the heart, lungs, liver, spleen, omentum, mesentery, kidneys, and spinal cord, and that the ecchymoses of the surface had resulted from the escape of blood into the skin and the subcutaneous tissues. The utter inadequacy of a diagnosis of Bright's disease of the kidney in such a case as descriptive of the real conditions is so plain that it must be evident to any one who has carefully considered the subject. Sometimes such a death seems like the natural result of the advance of years, the machinery wearing out simply because it is too old; or, again, it is as if premature old age came upon the patient, or perhaps he is worn out by dissipation, or by some physical labor so severe that it necessarily speedily exhausts his vital forces and produces physical disorganization. In order to draw the full measure of profit from the case it must be studied from three aspects,—the clinical history, the post-mortem examination, and the microscopical study of the tissues. The case would have been looked upon, if the symptoms had been considered in the ordinary way, as one of Bright's disease, and all the symptoms and lesions grouped around the kidney as the point of origin. The beginning with shortness of breath, soon followed by dropsy, and then the discovery of albumen and casts in the urine, and the various succeeding events in the history, are all the ordinary ones of Bright's disease. But to suppose, because the kidney was contracted, that the disease of the heart, of the lungs, of the blood-vessels, and the multitudinous other lesions were all secondary to the kidney disease is without any warrant in reason. Nothing is known even to show that the disease of the kidney was of older date than that of the other organs, and the succession of the symptoms would indicate rather the contrary, for the first thing noticed was shortness of breath on going up-stairs. If the subject be looked at without prejudice, there is nothing really known to show that dropsy is due to disease of the kidney. The multiplicity of lesions in such cases is very great, and it is impossible to distinguish the direct cause. If kidney disease does produce dropsy it can be only as a secondary result induced by some effect which the kidney is able to produce upon the more distant parts. But to return to that which more directly concerns the question of diagnosis and what may be learned from the case detailed. There can be no question that the symptoms indicated clearly the existence of disease of the kidneys and of the heart and arteries. The lungs

presented diagnostic features usually considered to denote hypostatic congestion or œdema or a slight degree of hydrothorax. There was no evidence of disease of the liver, and percussion of the splenic region revealed an absence of even the usual amount of dulness. As has been said, it is usual to set up the kidney disease, which is easily ascertained to exist if albumen and casts are found in the urine, as the central point, and to make everything else turn upon this. Various theories have been brought forward to show how the kidney disease produces an effect upon the arterioles, which in their turn become diseased and affect the heart. Long and complicated explanations have been written showing the intimate connection of the heart and the kidney through the circulation, and the reaction of the one upon the other, and how disease sometimes has its origin in the heart and extends to the kidney and again arises in the kidney and extends to the heart. Some of these theories read like romance, and are so beautiful that they lead one astray, until the time arrives to apply them in diagnosis and to fit them in with the post-mortem lesions, and then they are found wanting, for nothing is known to enable one to discriminate which of the organs first became diseased, or that the disease of any one of them was the cause of disease of another. It has been pointed out that there was objective evidence of disease of the kidneys, heart, arteries, and lungs, and this was so obvious during the life of the patient that it was easy to be sure of the existence of disease of these organs. To one, however, who has carefully considered cases of this nature, and has had a large experience, the clinical history tells a story which renders it possible to make a much more comprehensive diagnosis. In the first place, in regard to the blood-vessels, they are so universally diseased in Bright's disease, chronic heart disease, and all allied conditions that it is always safe as a part of the diagnosis to infer that they will be found to be involved, and, as a general thing, extensively. In the case related there was objective evidence of a calcareous condition of the radial and femoral arteries, and this made the existence of vascular disease even more certain than would have been the case if these external proofs had been wanting, as frequently occurs. The post-mortem examination showed how extensive this involvement of the arteries was. In the chapter upon the blood-vessels it has been shown how very frequently they are involved, and that there is every reason for supposing that the vascular changes play an important rôle in chronic disease and are not a mere incident in the disease of

the various organs which are involved. It is desirable therefore, in making a diagnosis, to try to form an estimate of the condition of the blood-vessels, for beyond doubt they have an important influence in chronic disease. It has been pointed out in the chapters on the disease of age and on the blood-vessels that disease of the latter is the inevitable result of the advance of years, and frequently occurs at all periods of life.

The kidneys were known to be diseased because albumen and casts were found in the urine. Although many curious and interesting things in regard to the urine have been discovered of recent years, the existence of albumen and casts taken in connection with the presence of general dropsy and the signs of enlargement of the heart still indicates positively disease of the kidneys, if there is anything positive in diagnosis. When this has been said, all that there is to tell of the state of the kidneys has been told, for there is no way to ascertain during the life of the patient what is the nature of the disease, or even whether the kidneys are enlarged or contracted. The albumen and casts, it is reasonable to believe, indicate the existence of some degree of inflammation at the time they are present in the urine. The various theories that have been propounded and around which classifications have been built—that the passage of large amounts of urine indicates one kind of disease and a low specific gravity another, that this kind of casts denotes one form of disease and that another—are useless, and will be found not to yield indications that will square with the post-mortem lesions. After much study of the question, there is only one thing which it is possible for me to declare with any degree of positiveness, and it is that in almost all chronic cases in which the kidney is involved it is safe to diagnosticate a greater or less degree of morbid fibrosis. In the chapter on the kidney the various forms of fibroid deposit have been illustrated, as well as the manner in which it has its origin.

The evidence of disease of the heart in this case of Bright's disease was most positive, for in addition to the murmurs which were detected, and which denoted injury of the valves, the impulse of the heart was diffuse, although not very forcible, and this indicated enlargement of the heart. No diagnostic indication can be more positive than that afforded by an increase of the area of the cardiac impulse, taken with the peculiar sensation imparted to the hand when it is placed over the heart, when it is of increased size. One must not be deceived by the effect produced by palpitation and

irregularity of the cardiac action. The heart seems to beat over an increased area and its action is very violent, but, ordinarily, this does not last a long time, seldom more than a few days, whereas the heaving and the extended impulse caused by actual enlargement are always present, and the sensation they impart to the hand is generally easy to recognize after it has been frequently felt. There is an important exception to the rule that an enlarged heart produces a heaving impulse perceptible over an increased area,—namely, that in the later stages of disease, when death is near, the heart becomes so weak that even when it is of enormous size it fails to produce such an impulse. It frequently occurs that patients are brought to hospitals in the last stages of disease and the physicians are called upon to make a diagnosis without knowing anything of the previous condition or history. Under these circumstances, when the cardiac action is very feeble, it is often impossible to form any just estimate of the size of the heart. There is no other change which the heart can undergo more important to recognize than its enlargement. The state of the valves is in comparison unimportant, for it is well known that persons suffering with valvular disease often live out their natural lives. On the other hand, when the heart is greatly enlarged life is seldom very prolonged. It has been pointed out in the chapter upon the heart that enlargement of it means disease of the walls, and the opinion expressed that what is called compensatory hypertrophy has no existence. Various forms of degeneration of the heart-muscle are there also illustrated and commented upon.

With regard to the lungs in the case under consideration, the diagnostic indications that they were diseased were sufficiently plain. It would be easy to say that the results of percussion and auscultation indicated the existence of hypostatic congestion of the lungs, and that the post-mortem examination showed this conclusion to be correct, and let the matter rest there; but it has long seemed to me that the lungs take a very important part through the course of Bright's disease, that they generally have a preponderating influence in causing death when it comes, and that they frequently are pointed out by the clinical history as the organs first diseased. It has been shown that the failure of the lungs to perform their function is the most common cause of death, much more common than failure of action of the heart or of the brain, the only other organs whose cessation to act immediately kills. Such being the case, it is unnecessary to explain further the necessity that diagnosis should be

as accurate as possible in order to ascertain all that can be learned during life in regard to disease of the lungs. The case under consideration presents the opportunity to illustrate diagnostic points of great importance, and therefore they may with advantage be passed in review somewhat at length. The results of percussion and auscultation were such as are most common in Bright's disease or in any of the combinations of heart, lung, and kidney disease which in practice are so frequently encountered. They were as follows: dulness on percussion at the bases of the lungs posteriorly, greater on one side than on the other, and at the areas of dull percussion almost total absence of breath-sounds,—an unnatural silence. At the middle portions of the lungs there were some crackles, and at the apices fairly good breath-sounds. No note was made of the condition of the vocal resonance and fremitus, which was an oversight, but under the circumstances both the fremitus and the resonance are usually greatly diminished at the bases posteriorly corresponding to the area of dulness. This condition has been so frequently found by me in other similar cases as to satisfy me that, if a note had been made of those diagnostic features, the vocal resonance and fremitus would have been found diminished. One other point was mentioned which is of great importance, although it seems a little thing: there was pain on percussion. Dulness on percussion at the bases of the lungs, weakness or absence of the breath-sounds, and diminished vocal resonance and fremitus are commonly accepted as the indications of hydrothorax. In this case there was none. Long experience with cases of this description has forced me to the conclusion that it is an error to believe that this combination of physical signs necessarily indicates the presence of fluid in the pleural sacs. I am convinced they are more frequently produced by disease of the lung itself. It is usually taught, and is true, that when the lung is solid there are, with the dulness on percussion, an increase of the vocal fremitus and resonance, and bronchial breathing. On the other hand, little is said and still less commonly taught of the physical signs which should be expected to be present when the lung is in such a condition as in the case under discussion, which is the state most common in Bright's disease and toward the later stages in most chronic diseases. Examination both macroscopically and with the microscope of a great many such lungs has shown me that there is a combination of blood-corpuscles, exudate-cells, and fluid in varying quantities in the air-sacs. Those who have examined many such lungs after death will recollect their soggy

condition, how freely fluid runs from them when they are cut, and their dark bluish-black color like that of clots of venous blood. When examined with the microscope large areas are found in which the air-sacs are filled with exuded blood-corpuscles or with amorphous material that was evidently mingled with liquid or semi-gelatinous serum, such as runs or can be squeezed from the lung when it is cut. Commingled with all this unnatural material filling the air-sacs is generally to be seen a greater or less number of the large cells called exudate-cells. Such lungs give physical signs identical with those caused by the effusion of liquid into the pleural sacs, and it is often impossible clinically to distinguish which of the two conditions is present, or whether, as often happens, the two coexist. It seems no more than might have been expected, when one stops to consider, that liquid in the pleural sacs and liquid in the lung itself should produce identical physical signs, and the conditions called œdema of the lung and hypostatic pneumonia are simply the results of the effusion of liquid or semi-liquid material into the air-spaces of the lungs. The purpose of all that has just been said is to direct attention to the fact that it is a diagnostic error to attribute to hydrothorax the combination of physical signs mentioned. Although a small amount of fluid is sometimes present in the pleural sacs, oftener there is none, and even when there is some pleural effusion the lung partakes in the disease process, liquid having escaped into the air-sacs. For all practical purposes there is no such thing possible as a simple hydrothorax as a complication of Bright's disease, the lung being always to a greater or less degree involved also. In diagnosis, therefore, it is always safe to infer, if it be ascertained that there is fluid in the pleural cavity, that the lung partakes in the process and is not simply forced aside and compressed by the liquid. Another physical sign which existed and has been said to be of importance was pain on percussion. This sign will be found to indicate almost infallibly the presence of pleurisy. Some degree of pleuritic inflammation and adhesion is almost universally an accompaniment of chronic disease of the lung, and therefore it might be said that it may be inferred to exist without there being any direct sign to indicate it. The examination, however, of many cases has shown me that when there is marked pain on percussion the pleural inflammation is extensive. It should be remembered that in the case under consideration the pleural adhesions were universal and the pleura was greatly thickened. In consumption, as well as in ordinary inflammatory affections with the lung involved, the presence

of pain on percussion will be found to be an important diagnostic sign of extensive pleurisy and pleuritic adhesions.

Much more might be said of the diagnosis of disease of the lungs, particularly in regard to the erroneousness of the prevalent belief that in cases of pneumonia the vocal resonance and fremitus are generally increased. If the term pneumonia is made to include all the ordinary inflammations of the lungs, the vocal resonance and fremitus are diminished in the majority of cases. There is only one form of pneumonia which causes increase of the vocal resonance and fremitus, the form which produces hepatization, in which the lung is unnaturally hard and tends to be dry. Most of the cases of pneumonia or inflammation of the lungs that are encountered are not of this variety. The lung is found to be here and there solid, but scattered through the solid portions are sacs still filled with air, so that often no part of the lung will sink in water. The material filling the air-sacs can be squeezed out to a great extent by pressure with the fingers, and the tissue does not tear easily, as hepatized lung does. Examination with the microscope shows the material in the air-sacs to be a mixture of blood-corpuscles, exudate-cells, amorphous material which is visible, and other matter which appears as empty space, being unstained. There is generally no fibrin to be seen under these circumstances. The physical signs produced by this form of lung-inflammation are impairment of the percussion sound, but not flatness, feebleness of the respiratory sounds, but no bronchial breathing, and diminished vocal fremitus and resonance. The conditions are rather negative than positive, for often both lungs are involved and therefore a good lung cannot be compared with a diseased one. There is frequently only slight impairment of the percussion resonance, and as this is on both sides there is nothing to compare, and it is therefore hard to be sure of it. When the breath-sounds are listened for, there is a curious silence, and it is difficult to determine whether this is because sounds cannot be produced or because the patient will not breathe, and then, perhaps, the vocal resonance and fremitus seem to be diminished. Such a condition is of frequent occurrence in practice, and it is as much a pneumonia which will occasion fever and take away the strength and force the patient to go to bed, as is the form in which the lung becomes hepatized and all the classical signs that can be elicited by percussion and auscultation are present. This theme of the diagnosis of pneumonia could be pursued to much greater length, but it might lead too far from our subject.

The case selected as a type has now been discussed so far as concerns the objective signs of disease brought to light by the clinical history and physical examination. These made evident that there was disease of the heart and of the blood-vessels, of the lungs and of the kidneys. No other direct evidence of disease existed, and the case might have been called Bright's disease, and its study pursued no further, it being assumed that the process had its origin in the kidney and thence extended, the involvement of the other organs being a direct consequence of the disease of the kidney. It has been said that the theories which make disease of the kidney the cause of so much disease of other organs have no firm foundation, and from the diagnostic stand-point totally fail to explain most of the common phenomena of Bright's disease. Bright's disease is now well known to include extensive involvement of other organs besides the kidneys, and should no longer be classed simply as a disease of the kidney. It is possible in diagnosis to go far beyond that which can be known from objective signs and symptoms alone. Much may be inferred as a matter of general principle of what must occur in organs which yield no external sign recognizable during life. The physician who would have the most comprehensive grasp upon his cases must keep ever in mind that after all available methods of diagnosis have been exhausted there still often is disease which, having eluded discovery during life, was not recognized at the post-mortem examination, and was brought to light only by the use of the microscope. The case under consideration illustrates this. The history shows that the hepatic dulness was not increased, and that there was tympanitic resonance in the area of ordinary splenic dulness. It has been again and again mentioned in the previous chapters that fibrosis is an essential part of chronic Bright's disease, and that it is seldom confined to a few organs, but is usually widely spread. In such cases, therefore, it is a fair diagnostic inference to make that when the heart, blood-vessels, lungs, and kidneys are diseased the liver and spleen will not escape. Although there was no external diagnostic evidence, it was safe to predict that the liver and spleen would be found diseased. The post-mortem and microscopical examination showed this to be the case, and the illustrations (Figs. 85 and 89) demonstrate the fibrosis of both of those organs. In interpreting the results obtained from physical examination of the liver and spleen it must be remembered that percussion and palpation, which are the only available methods, yield at best very imperfect indications and give no informa-

tion whatever in regard to the slighter changes. When the liver is greatly enlarged or very small it is often possible during life to be pretty certain of it, but when, as happened in the case under discussion, the reduction in size is very slight, it is impossible to find this out, although the organ may be greatly diseased, as was indeed the fact. The spleen being of small size and hidden within the cage of the thorax, information in regard to its size obtained from physical examination is still less reliable. In the type case there was no splenic dulness, which would have seemed to indicate that the organ was small, and yet post mortem it was found to be of normal size and greatly diseased. Even if it had been possible during life to know that it was of normal size, the fact that it was diseased would still have remained undiscovered. The lesson which it is intended to emphasize by what has been said of the liver and spleen is that all the available methods of physical diagnosis should be employed, but that it is still more important to remember the habit of chronic disease to produce wide-spread effects, and, therefore, that more may often be learned of the condition of these organs from general inference of what must occur if the blood-vessels, heart, lungs, and kidneys are diseased than could be learned directly from percussion and palpation.

The second fact, that important lesions may exist and fail to reveal their presence by clinical symptoms and elude discovery at the post-mortem examination, to be demonstrated only by the use of the microscope, is illustrated by what was found in the spinal cord. There were no clinical symptoms of disease of the nervous system, and at the post-mortem examination the brain and spinal cord appeared to be normal. The illustrations (Figs. 127, 128, and 129) show how false would have been the conclusion that they were really healthy. It is unnecessary here to discuss the nature of the disease, for this has already been done in its appropriate place in connection with the illustrations in the chapter on the spinal cord.

What, then, are the lessons which should be learned from the case which has been related and commented upon from so many points of view? It emphasizes in the most positive way the inadequacy of the view that Bright's disease is essentially a disease of the kidney. This was discussed by me in an essay published some years ago.*

There are three salient points to be kept in mind in diagnosis:

* A Study of the Arteries and Veins in Bright's Disease, by Arthur V. Meigs. Transactions of the College of Physicians of Philadelphia, 1888, and Medical Record, July 7, 1888.

first, all available methods of investigation must be employed which can directly indicate disease of the organs, and these must be brought to bear upon as many of the organs as possible; second, owing to the habit of chronic disease to produce wide-spread effects, it is generally possible to draw inferences of the existence of disease which reveals itself by no external indication; and, third, owing to this same habit of chronic disease to spread itself over a great extent of the bodily territory, there are often lesions which the microscope alone reveals, they having made no sign by clinical symptoms, nor been visible to the naked eye at the post-mortem examination.

The diagnostician who shuts his eyes to the revelations of pathology during the last thirty years,—to all that has been learned since Gull and Sutton put forth their classic observations on "arterio-capillary fibrosis,"—and continues to regard disease from the earlier stand-point, must fail to understand the chronic cases that have the misfortune to fall into his hands. The puzzle in diagnosis often encountered, to decide which is the primary disease, when it has been ascertained that there is in a given case organic disease of the heart, lungs, and kidneys, is frequently insolvable. The name Bright's disease has now long been given to cases with albumen and casts in the urine and dropsy. With these symptoms it has been found, as time has passed, that there are generally associated disease of the blood-vessels, of the heart, and of the lungs, and occasionally convulsions called uræmic, and sometimes insanity. Close scrutiny reveals that at one time or another disease of almost every one of the organs and the symptoms of every known form of chronic disease are found associated with what the puzzled diagnostician cannot escape from calling Bright's disease. The pathological condition common to all the organs thus invaded is an increase of their fibrous tissue, and with this vascular disease is almost universally associated. One of two things is almost certain to happen: the term Bright's disease will be made to include a much more extensive range of disease than it originally covered, or it will disappear from the accepted nomenclature. The latter is much the more likely to occur, although it will never be forgotten that Bright's discoveries marked an important advance in medicine. For the diagnostician cases of chronic disease with involvement of many organs present great difficulty so long as his work continues hampered by the older views of the subject; to reach a position where a reasoning mind can rest with any degree of satisfaction it is necessary to cast aside many theories that have been long received, and to give up

comfortable explanations of things that are hard to understand. The state of knowledge at the present time is about this: the wide-spread disease of the tissues and organs in the conditions under discussion is well known, and it has been ascertained that the pathological lesions which form an invariable accompaniment are varying forms and degrees of fibrosis and vascular disease. With the progress of time and the advance of knowledge so much has been included by the name Bright's disease that the term will no longer cover all that it is attempted to place under it. It is manifest that to talk of disease of the kidney is quite aside from the facts in many cases, for often the kidney does not bear any important part. Of the ulterior causes of chronic disease something, but by no means all, is known. There can be no doubt that the passage of time produces it, the fibrosis which is inevitable to age coming sooner or later in every one not cut off in some accidental way, and with the fibrosis come those forms of inflammation to which morbidly fibroid tissues are prone: the combination of fibrosis and inflammation constitutes the disease. It is equally certain that dissipation, unhealthy modes of living, and what appears to be an inherited disposition to premature decay can produce the same or very similar effects even in young persons. The relations of other forms of disease, which at first sight appear to have nothing in common with the ordinary chronic diseases, have been discussed in some of the preceding chapters. The purpose of the last few pages has been to emphasize the statement that the diagnostician must learn to regard such conditions as that presented by the type case of Bright's disease which was given, and many cases of disease of other of the great organs, as but the varying expressions of the same process. Although this strange and wide-spread process is very imperfectly understood, enough is known to make it necessary to acknowledge its existence. One chapter has been devoted to the citation of the facts showing that there is such a thing as the disease of age; again, it has been argued that, owing to the operation of various causes, some of which were named, there arises a state of disease which was likened to age in youth. It has been pointed out that both the last-mentioned states are recognized by the diagnostician as Bright's disease. Pathology gives the information that the lesion invariably present in all is fibrosis. It seems, therefore, only reasonable to call the disease fibrosis, with the reservation that it is certain that final knowledge has not yet been even approached, for there must be some great underlying cause which still remains hidden.

There are other states of disease which it is necessary for the clinician to recognize and classify by diagnosis. It commonly happens that cases are met with in which the history and physical signs appear to indicate clearly that the heart was first diseased and afterward the other organs became involved. Often, as such a case progresses it presents the entire clinical picture of Bright's disease, but neither albumen nor casts at any time appear in the urine. It even happens that the urine is passed in normal quantity and is of normal specific gravity. What diagnosis is to be made under these circumstances? It has occurred to me a number of times in such instances to find at the post-mortem examination the kidneys contracted and cystic,—types of fibrosis. Several important lessons are taught by this. It is a fair diagnostic inference that the kidneys will be more or less fibroid when the other great organs are so diseased, and this will be found to be seldom erroneous. The inference is precisely parallel to that which it has already been pointed out may be made in regard to the liver and spleen in the absence of objective evidence of their being diseased. The kidney is frequently diseased when there is no evidence of it to be obtained from examination of the urine, and this is an important fact to be kept in mind in diagnosis. Such a case constitutes another link in the chain of proof that the term Bright's disease has grown to cover an enormous extent of disease, and that there is every reason to suppose the kidney plays a very minor rôle, being only more important than the liver and the spleen, and immeasurably less so than the heart and the lungs, and occasionally the brain. In the same way that it happens that the heart is the first organ to be attacked in cases which subsequently present the clinical picture called Bright's disease, it frequently occurs that the lung is first involved. An attack of catarrhal pneumonia or a predisposition to take cold, with numerous colds during the course of a year or two, in a person previously perfectly healthy is frequently the opening to a chronic illness which sooner or later takes the form of Bright's disease and ends in death. Jaundice or other disease of the liver may mark the beginning of such chronic disease. From the point of view of diagnosis such cases are sometimes very puzzling, and were formerly, when Bright's disease was looked upon as essentially a disease of the kidney, more so than at present, since a more comprehensive view is now taken. In these combinations of disease the diagnosis must be pursued along the lines already indicated, all methods of physical examination being exhausted to ascertain the condition of as many of

the organs as possible, and from this inferences drawn in regard to disease of parts that give no external sign; and it must be remembered that even after this has been done there will still remain lesions that are discoverable only by microscopical examination.

Perhaps the most extraordinary clinical picture is that presented when the nervous system is first attacked. This subject has already been mentioned in the chapter on the spinal cord. Of more recent years a number of essays have appeared, written by alienists, directing attention to the connection of insanity with Bright's disease. This goes to show that the brain as well as all the other great organs is liable to suffer in the course of chronic disease, and that it as well as any of the others may be the first to be attacked. It is not a rare occurrence in practice that insanity is developed in the course of Bright's disease, and alienists now allege that the two frequently have some connection. This makes it highly probable that the fibrosis and vascular disease which are found widely extended in the bodily organs will soon be discovered to be as frequently present in the brain. It has happened to me a number of times to see cases in which disease of the spinal cord was inextricably mingled with general chronic disease. In some of them there was clinical evidence of disease of other organs before that of the cord manifested itself, but in two the spine was the first organ to show itself to be diseased, and there were other clinical phenomena of such unusual or obscure nature as to make one of the cases worthy of discussion at some length.

A man who died at seventy was throughout his life very healthy. Twelve years before his death he had an attack of catarrhal pneumonia following exposure, but recovered completely. Between two and four years afterward, and so gradually that a more exact period cannot be fixed, he began to fail. This took the form of weakness of the legs, so that walking was disagreeable, and then difficult. His gait was uncertain and shuffling, the feet not being lifted naturally from the ground. This condition of the legs increased until he could walk but little, and occasionally had falls owing to slight causes; then he gave up walking almost entirely, and at last was unable to walk without assistance. Upon several occasions he was impelled to run (a symptom not uncommon in spinal disease), and once or twice fell, at other times saving himself by seizing some fixed object, which he held until his equilibrium was regained. His gait was neither ataxic nor spastic, but rather one of mistrust of his power of equilibration,

the steps being short and shuffling. The sense of touch was not impaired, and the reflexes of the tendons of the patellæ were absent. Three years before his death all the muscles of both lower extremities were found to react to the slowly interrupted faradic current. Of the left leg the reaction to the rapidly interrupted current was very poor, and to the slowly interrupted current much more feeble than the reaction of the right leg. The muscles were weak, small, and flabby. More than once he lost control of his rectal sphincter. The bladder performed its function naturally. The urine was examined occasionally in various years, and neither albumen nor casts were found, and when the specific gravity was taken it was normal, or above the normal. The mental as well as the bodily condition seemed involved in the process of decay. He was never in the slightest degree insane, but became crotchety, irritable, and mentally inefficient. At times the pulse was very irregular and the digestion disordered, but, as a general thing, through the whole of the eight or ten years of illness the bodily health was fairly good. Physical examination never developed signs of disease of any of the organs. For some months or perhaps even for a year before death there was some pain upon any attempt to make a movement, especially of the left arm, and during the last week or two the pain on movement was intense and to move the left arm caused agony. During the last two or three weeks, in addition to the weakness of both the legs there was partial left hemiplegia, and he fell into a stupor. A few days before death he expectorated some bloody mucus. The respirations became shorter and the pulse weak and irregular; finally the lungs filled up, and he died. At the autopsy, which was made twenty hours after death, the spinal cord looked a little small and was somewhat flabby, although it was not especially easily torn or crushed. On section it was seen that the separation of the gray matter from the white was less sharply defined than is natural, and the gray matter seemed to be reduced in amount. On opening the thorax and abdomen it was perceived that there was an enormous accumulation of fat. It lay in the thorax, in the pericardium, and upon the heart, in the omentum, and throughout the abdominal cavity. The heart presented no marked evidence of disease except the very thick layer of fat upon its surface and slight fibrous thickening of the aortic leaflets. The lungs at their posterior portions were almost black, and here and there non-crepitant, but the greater part of them was crepitant. The liver presented no gross evidence of disease. The spleen was small and whitish, and

the capsule a little thickened and wrinkled. On section the organ appeared to be fibroid. The kidneys were of only half the natural size, and embedded in great masses of fat, which were nine inches in the longer by five in the shorter diameter. On attempting to separate the kidneys from the fat the capsules stripped off, remaining with the fat, and the blood-vessels which pass in through the capsules appeared to be both numerous and enlarged. The surface of the kidneys was rough and granular, and on section it was seen that in addition to their diminished size the amount of the cortical substance was greatly reduced. The muscles of the body and limbs were shrunken and small, and there was a great accumulation of fat. Microscopical examination of the heart, lungs, liver, spleen, and kidneys revealed the existence of fibrosis of all these organs and extensive vascular disease. If a type of granular kidney were sought it would be difficult to find a more perfect one than was exhibited by these organs, and the disease of the blood-vessels was so marked and of so peculiar a type that one of the arterioles has been used for illustration (Fig. 14). In connection with the picture will be found a fuller description than it is desirable to introduce here under the head of diagnosis. The study of the cord with the microscope was most fruitful, and demonstrated the presence of lesions which are not generally described, and from which important deductions both in regard to disease in general and to diagnosis in particular may be made. A number of the illustrations (Figs. 134 to 137) are from sections of this cord, and these are described in their appropriate places in connection with the pictures.

This case as it has been related is the antithesis, from the standpoint of diagnosis, of that which has been given (page 174) as typical of Bright's disease, and yet the post-mortem lesions, although they varied in many details, were so much alike as to make it seem that both were instances of the same disease. Although the symptoms of disease of the spinal cord were the only ones that ever existed, there was something in the condition of the patient which made me feel assured for several years before his death that there was disease of the kidneys and of the heart and lungs. It is most important for the diagnostician to know that such a combination of conditions as occurred in this case is possible. The accepted signs of disease of the kidneys, although sought, were always absent, even the specific gravity of the urine, which is said to be low in contracted kidney, having been, when taken, normal or above the normal, and yet it was possible to make the diagnostic inference that the kidneys were fibroid. This

was done simply as a matter of general principle, of deduction from what had been found by experience in other similar instances,—that in a man with such marked evidence of degenerative disease of the spine, the process having lasted through years, there must be a generalized fibrosis. When there is generalized morbid fibrosis no organ is more likely to suffer than the kidney. The failure of the specific gravity to fall below the normal is a most important point in diagnosis, for it is taught in most text-books, and very generally accepted as a fact, that no other single sign is so unfailingly present in cases of contracted kidney as low specific gravity of the urine. This has long seemed to me to be an inference founded upon insufficient evidence. Now that there is tangible ground for it, although only one case in point is offered, it is time to assert that the specific gravity is not always low in contracted kidney, and that other and better methods of establishing the diagnosis must be sought. This means is much more likely to be found in a careful estimate of the probable general bodily condition and deductions therefrom in regard to disease of particular organs than by a narrow adherence to any doctrine of what ought to be the specific gravity of the urine. A symptom which was mentioned in the history, and which is worthy of further consideration, is that there was pain upon motion of the extremities for some time before death. The symptom is a common one in this form of disease of the spine, and it often constitutes a striking feature during the last few weeks in aged persons who die of chronic disease. It must be the result of inflammation of the spine or its meninges, and it presents many points of resemblance to the general hyperæsthesia which is one of the ordinary features in cases of acute meningitis. Clinically the case was one of spinal disease pure and simple. After all methods of diagnosis had been exhausted, no direct evidence of disease other than that of the spine could be obtained. Inference alone led to the conclusion that other organs were involved, and the case lends support to the view, which it has been my desire to make felt at every point throughout this work, that chronic disease is always wide-spread in its effects. Although clinically a case of spinal disease, it had all the characteristics, if examined from the side of the post-mortem alone, of Bright's disease. This aspect of the case having now been sufficiently emphasized, it remains to ask how it should be regarded as concerns its classification as a spinal disease. What diagnosis should have been made after consideration of the various symptoms and from the results of physical examination?

These did not accord with any of the descriptions in text-books of the various forms of spinal sclerosis or of myelitis, and the post-mortem examination and results of microscopical study as shown in the illustrations were not those belonging to any of the ordinary classified diseases. It might be well to give a new name to this form of disease, the spinal fibrosis and degeneration that accompany Bright's disease and which are almost parts of it. So far as concerns the lesions of this curious degeneration, it is not necessary to describe them here, as this has already been done in connection with the illustrations. (Fig. 134 to Fig. 137.) The diagnosis, the history, and the symptoms of the case have already been detailed in full (page 188). It has been my lot to meet with this condition of the spinal cord a number of times, but only in one other instance have I met with it in a form parallel with that of the case which has been given in full, in which the spinal symptoms were the only ones manifest during life, and yet the lesions of extensive generalized disease were found at the post-mortem examination. In that case there was strong reason to believe that syphilis was the underlying cause. In other cases the same symptoms of spinal disease, the curious dragging of the feet, uncertainty of equilibrium, and finally incomplete paraplegia of the legs, appeared as complications in persons suffering with the ordinary conditions observed in Bright's disease. The disease is one in which the lesions occupy all parts of the spinal cord, and are not confined to particular regions as in the spinal diseases usually described, and the symptoms do not conform with any of the ordinary types.

In practice it is not rare to meet with cases of illness in which there is prostration and even fever and yet no satisfactory reason for the attack can be discovered. It has happened to most clinicians, probably, to have this experience. Such an attack may last for many weeks or even longer, and after it is over no explanation be forthcoming. Without doubt there is always a cause, and it is probable that processes are taking place somewhere in the body resulting in the production of lesions that would be visible to the unaided eye or could be seen with the microscope if it were known where to look for them. It has happened to me again and again to see such attacks of sickness, and my mind has been forced to the conclusion that they must often be the occasion of organic lesions. It has been stated a number of times in the chapters dealing with the various organs that lesions which were quite unanticipated are often found. It is a fair diagnostic conclusion in these vague cases, especially when they are

of any great degree of severity, that some inflammatory or degenerative process is taking place and will result in organic lesion.

That mistakes in diagnosis are made no one will deny, and sometimes the symptoms are so misleading that they cannot be avoided. One disease so closely imitates another that it is impossible to avoid being misled. It has been pointed out how wide-spread chronic disease is in the effects it produces, and it is certain that chronic processes usually latent in their mode of progress are liable to occasion acute and even violent outbreaks in one part or another. It is important for the clinician to keep this fact in mind, for the symptoms of some one of the acute diseases may be so closely imitated as to give rise to a mistake in diagnosis. This recalls a case of perihepatic abscess the outcome of long-standing chronic disease which was mistaken for typhoid fever. The liver from this patient has been used to illustrate certain peculiarities of disease of that organ (Figs. 76 and 77), of which a description will be found in connection with the pictures. The man was sick for several weeks with what seemed more like typhoid fever than anything else; at any rate, no other diagnosis could be made, and it was only the post-mortem examination that revealed the presence of a large perihepatic abscess and chronic lesions that must have existed a long time before the abscess which was the immediate cause of death. The fact is interesting that these wide-spread chronic lesions may give rise to acute inflammatory outbreaks, and it is very important, from the diagnostic point of view, to remember that such a thing is possible. Mistakes may be made even in a disease of such definite nature as typhoid fever is commonly thought to be. It has already been pointed out that there is some reason for believing typhoid fever to be a less definite entity than it is generally considered, and that nature does not draw abrupt lines separating one disease from another to such an extent as is usually believed.

A singular fact, and one worthy of consideration, is that a sudden violent diarrhœa or cholera morbus in an elderly individual not usually subject to such attacks is generally an indication of the existence of organic disease. Such organic disease often has been entirely latent, and the first intimation of its existence is the unexpected attack of intestinal disorder. So often has an experience of this kind come under my notice that it is not putting the matter too strongly to say that a sudden intestinal attack in an elderly person not previously subject to such attacks should always be considered a

reason for setting in motion every diagnostic method of search for organic disease. If nothing is found, it is a safe inference that such disease exists if the attack was violent and if there is no other reason to explain it. It is not rare that an acute attack of diarrhœa or of cholera morbus gives the first intimation of the existence of grave organic disease of the heart or of Bright's disease. The cause of this connection between acute intestinal attacks and serious disease of the organs cannot now be explained, but the lack of an understanding of it is no reason why the connection should not be kept in mind and utilized in diagnosis.

If an acute intestinal attack in a person not subject to such attacks should be considered as a warning of the existence of some disease, the occurrence of epistaxis in an elderly person not subject to nose-bleed should be regarded by the diagnostician with even more suspicion. It is an almost infallible sign of organic disease. There is no occasion at present to discuss extensively this curious fact, which cannot now be completely explained. Although nose-bleed occurring after middle life is frequently a sign of organic disease, it is not intended to say that it is impossible for uncomplicated epistaxis to occur, but simply that in practice when an elderly person not constitutionally subject to it has nose-bleed, especially if it be severe, it will almost always be found that there is organic disease. The diseases most commonly found under the circumstances are kidney disease and organic heart disease, but in my experience the latter is less common. The association of epistaxis and heart disease is an old and well-known clinical phenomenon. It must be that such nose-bleed is due to organic change of the walls of the supply-vessels, for it is not conceivable that healthy vessels would rupture without cause. That disease of other organs should be brought to light in this way is another proof of the wide-spread nature of the lesions of chronic disease, but the diagnostic point to be recollected and to be here emphasized is that when such epistaxis as has been described occurs, the diagnosis of organic disease may generally be made. The form that will be most frequently found is disease of the kidney. It would be difficult to exaggerate the importance of this diagnostic inference, and it may be added that if thorough examination of an elderly person who has had severe epistaxis fails to lead to the detection of any disease, its existence should still be suspected until a sufficient time has elapsed to make it reasonable to suppose that good health is still maintained.

A common symptom in elderly persons is confusion of speech

with slight paralysis or paralytic weakness, rapidly passing away and leaving the individual just as he was before. Such attacks most frequently occur in persons past middle life, and study of their history generally brings to light that there had been some previous failure of health. Although this is not invariably the case, it is so in the great majority of instances. The question, What is the precise cause of such symptoms? is one which it is very desirable to answer. That, however, which it is most necessary to explain in a discussion of diagnosis is what should be inferred when a case of the kind is met with in practice. It is impossible at present to say with certainty what causes such attacks, but it seems hardly likely they can be due to apoplexy. It is difficult to believe that paralysis or confusion of speech caused by the rupture of a vessel and effusion of blood, which necessarily destroys some portion of the brain-substance, could pass away so rapidly as these attacks do. It has happened to me many times to see persons with slight facial palsy and difficulty of speech or confusion of mind which disappeared entirely after two or three hours. In most cases there have been a number of attacks in the course of two or three years. Sometimes an attack may take the form of difficulty in walking, or there may be confusion of mind or difficulty of expression in speech alone. Patients affected in this way invariably have failing health, and the end may be in an attack of apoplexy or Bright's disease or pneumonia or any other of the diseases to which elderly people are prone. As already said, it seems rather a far-fetched explanation to attribute the attacks to hemorrhage into the brain, and certainly there have been no post-mortem observations to support such a view. Clots are so often found in the blood-vessels in many parts of the system, and they are so commonly found in vessels of the smallest size, that experience has made me believe that clots in unruptured vessels are the cause of much more disease than is commonly known, and that they are often formed and afterward rapidly removed, leaving the vessel in a condition nearly natural. Such a theory if it could be sustained would explain the passing cerebral attacks which have been described. However this may be, it is certain that such an attack has an important diagnostic significance. It is a sign that may be relied upon of the existence of vascular disease, and that the vascular disease, as is its habit, is of wide-spread extent. In addition to changes in the blood-vessels which are inevitable to age, the diagnosis may safely be made of grave organic disease, and if no certain signs of it can at once be found, they will appear within a

year or two if the degenerative processes that have begun continue at their ordinary rate. Whether the disease which first manifested itself in the brain will continue its work there, or will break out in the heart, lungs, kidneys, or elsewhere, cannot be known if the examination of those organs fails to reveal the signs of disease. The diagnosis, however, of organic disease may safely be made, and time will show what form it is to take.

Recently much has been written of an unnatural increase of the intravascular blood-pressure. It is commonly spoken of as a clinical symptom of great importance, and as if it were an easy matter to ascertain its existence. This, however, is far from being the case. There can be no doubt that the heart, by the changing force of its action, can vary the degree of pressure within the arteries, and it is probable that other conditions also contribute to the same end; but it is equally certain that for the diagnostician nothing but the introduction of an instrument of precision into the blood-stream, as has been so often done in the lower animals, can give final information upon the point. It would not be desirable to attempt here to discuss in full this most intricate subject, but it may be said that many of the untenable theories which pass current lead to most unfortunate errors in diagnosis, and thus to wrong treatment, which is still worse. In the chapter on the blood-vessels it has been pointed out that the disease to which they are most liable is fibroid thickening of their walls, and every one knows how common enlargement of the heart is. It is when the heart is of increased size that the pulse most often has the character usually called "high tension." There are at least two reasons for thinking the so-called high tension character is often present when probably the blood-pressure is below instead of above the normal. The first of these is that the force with which an enlarged heart beats is often much less than the normal, and the second that arterial disease is often of such a character as to change the walls of the vessel so as to give the impression of a high tension pulse when in fact the blood-pressure is low. When the walls of an artery become thick it is impossible by feeling its pulsations to ascertain whether the peculiar sensation of hardness which is conveyed to the finger is due to stiffness of the walls or to an unnatural hardness of the column of blood that is flowing within it. The correctness of this statement may be verified by any one who will take the trouble to study during life the condition of the radial and femoral or other arteries that lie beneath the skin, and, having found vessels with the high tension character,

examine them, as the opportunity offers, post mortem. Extensive study carried out along the lines indicated has led me to conclude that the so-called pulse of high tension is unreliable as a diagnostic indication, and that it is probable that when it is present the blood-pressure is often low, this misleading result being brought about by fibroid thickening of the arterial walls. In the chapter on blood-vessels it was shown that the radial artery, which is the one from which the character of the pulse is most often judged, is peculiarly liable to become thick-walled. It is not necessary to dilate fully upon the misleading results obtained by feeling the heaving beat of an enlarged heart. The conclusion that such an organ pumps with unnatural force is often a wrong one, for the great impression produced upon the hand placed over such a heart may be due simply to the increased size of the organ and to its being too large for the space that contains it. It has been shown in the chapter on the heart that in cases of hypertrophy the walls are in most instances degenerated and probably weak instead of having increased strength. For the reasons, therefore, that an enlarged heart with a heaving impulse often is a very feeble pump, and that thick-walled arteries give an impression identical with that produced by increased intravascular pressure, the so-called high tension pulse is very unreliable as a diagnostic sign, and is often present when the circulation is feeble and inefficient rather than bounding and dangerously strong.

A most difficult question in diagnosis and one impossible at present to answer conclusively is, What is the relation of gout to Bright's disease? Although complete knowledge is as yet not even to be hoped for, the subject is so important, and in practice the two diseases, which in their typical forms of development are so utterly unlike, are so often found together, that the discussion of their relationship should not be avoided. There is no difficulty in recognizing gout in its typical form when it attacks the joints, and it is hardly necessary to say that Bright's disease when fully developed constitutes a very distinct clinical picture. The difficulty is encountered when one comes to deal with what are called "gouty tendencies," and sometimes to decide why gouty heart and gouty kidney are so named. The names were introduced to describe attacks of illness encountered in practice, and their very existence is an indication of the relationship of gout and Bright's disease. There are cases with symptoms so vague that no particular organ or part can be connected with the attack, and yet something suggests gout so strongly that it has

become the custom to speak of a "gouty tendency," though it may be impossible to say precisely why this is. On the other hand, local disease may appear in an unusual form and may last so long as to make it appear that there must be some constitutional fault to cause it: such attacks are said to be of "gouty origin." As an instance of the latter form of disease, a man or woman of fifty may have pain in the foot lasting for months or even longer and with only slight external evidence of disease. Such an attack may come after a trifling local injury, or there may have been no accident to account for it. There may be slight swelling or redness, or, again, no external evidence of inflammation. Very severe pain is complained of, and there can be no doubt that this is real, for persons so affected will refuse to use the affected foot at all, and remain bedridden or seated in a chair. Such disease is said to be based upon a gouty constitutional fault. Is it not more like Bright's disease local in the foot? The resemblance of the gouty constitutional taint to Bright's disease is very close. Much has been written, especially in Great Britain, of the gouty heart and of the gouty kidney. What are they but the heart and kidney of Bright's disease? It is the old, or the prematurely old, or the dissipated, who are so affected. After all, it is but old age or age in youth, the combination of fibroid growth with the process of inflammation, and all the infinitely various clinical forms are produced according to the respective quantities of the two ingredients—morbid fibrosis and inflammation—in the mixture. The practical lesson to be learned is that pathology has outrun diagnosis, so that the knowledge is forced upon us that diseases that have been considered to be distinct are related. It must be, too, that vascular disease, fibrosis, and the inflammations that are sure to follow in their wake have much to do with, if they are not the causes of, both gout and Bright's disease.

In the diagnosis of chronic disease it must be remembered that the beginnings are, in the nature of things, obscure. Many of the pathological lesions which are illustrated in the chapters on the various organs have their origin, and even attain considerable proportions, without manifesting their existence by any external sign. Another mode for their production is through vague attacks of illness which are difficult to classify. Such attacks have already been discussed in this chapter. It has been shown that the latent existence of these lesions is of very great importance to the individual, as in time they accumulate until in themselves they constitute grave chronic disease, or else if the person is seized by acute illness they have so lamed the

organism that they have a preponderating influence in determining a fatal ending of an attack that would not have killed a sound person. For the diagnostician nothing can be more important than to recognize chronic disease in its very origin. This can be done only by remembering that it is almost always wide-spread in its effects, and by the observation of very little things. There are no set symptoms, and it is largely by inference that a correct estimate can be made. Perhaps no one thing is more important for the diagnostician to know than that vascular disease and fibrosis are certain to come in all men if they live to be old enough. The corollary is that a similar state is produced earlier if the necessary conditions exist, and thus chronic disease resembles old age in youth.

CHAPTER XIV.

PROGNOSIS IN CHRONIC DISEASE.

PROGNOSIS will be dealt with like the various subjects heretofore treated. No attempt will be made to discuss it in full, but only a record made of such experiences as may aid to extend our power to forecast the future in disease and to correct errors. In chronic disease the prognosis is often much more gloomy than the occasion warrants, because when the conclusion has been reached that a case is incurable it is forgotten that it is not the question of its curability or incurability alone that should govern the forecast of the future. The fact that the patient is alive at the moment of examination establishes that his immediate state of disease is compatible with the continuance of life: the real question for prognosis is the rate of progress. In practice this most important consideration is commonly forgotten, and so soon as the diagnosis of incurable disease is made it is concluded that death is imminent. In a disease like cancer this conclusion is reasonable enough, for it is of comparatively rapid progress, and under all ordinary circumstances a few years put a period to the life of the individual attacked by it. The question, however, is very different in ordinary chronic disease: it has no fixed habit in its rate of progress. An individual suffering with chronic incurable disease may live indefinitely if the disease ceases to progress. Nothing probably could better illustrate this than what sometimes takes place with cataract, which may cease to grow, the person never becoming blind. Many unfortunate errors in prognosis have been made, inevitable blindness having been prophesied of persons with cataract who never became blind. Such errors are less common than formerly, because the specialists have learned that it is impossible for them to forecast the rate of progress, and that there may even be no progress. The parallel between fibroid disease and cataract may be carried further, for traumatic cataract may occur in early life. In that form it seems like age in youth as much as many of the chronic diseases which belong naturally to age but can under favoring circumstances be produced in youth. It has for a good while been understood that acute disease of the kidney frequently ends in complete recovery,

but chronic kidney disease is still generally considered to warrant a very grave prognosis, in most instances even that death will soon ensue. Chronic Bright's disease is considered both incurable and rapidly fatal. A few years ago skilled microscopists were willing to undertake to make a prognosis from an examination of the urine alone without having seen the patient and with no knowledge of his condition. If oily casts were found, it was announced that death would ensue within two years. The erroneousness of such a position is now thoroughly recognized, but even yet it is not so well known as it should be how long men who have had chronic Bright's disease live and even enjoy good health. The presence of albumen and casts in the urine continuously for any considerable time is a positive sign of disease of the kidney, but only a study to ascertain the state of the other organs and of the general condition can yield information sufficient to warrant a prognosis. On the other hand, it has been shown (page 190) that the most extensive disease of the kidneys may exist and fail to reveal itself by anything in the urine. To illustrate, two cases may be mentioned of men who were ill when about sixty years of age. In both instances there were albumen and casts in the urine during about two years. One of them had catarrhal pneumonia, and the other bronchitis and coryza. Both recovered and enjoyed good health afterward, one dying seventeen years later, and the other is still alive after twenty-one years, and is now more active than the generality of men of eighty. There can be little doubt that the kidneys were left scarred and injured by the disease so many years ago, and it is probable that in men so old this made constant latent progress, but the lesson taught is that a very grave prognosis is not warranted under such circumstances, for although the disease may have been and probably was incurable, its existence was not incompatible with the subsequent possession of good health. It is not rare to see attacks of jaundice in elderly persons accompanied with such symptoms as seem to indicate grave disease of the liver and at the same time the signs of general fibroid and vascular disease. Such attacks not rarely end in recovery. Under the circumstances there is probably severe inflammation of a part or the whole of a liver already lamed by fibroid and vascular change, and it is almost certain that the organ is left in worse condition than before the attack. The prognosis, however, should not be too grave, for even if the patient has incurable disease this will be of comparatively little importance if it remains latent, so that he can continue to enjoy comfortable health.

Few symptoms are more alarming and at first sight seem more positively to warrant a bad prognosis than excessive irregularity of the action of the heart. Great irregularity of the cardiac action when it lasts for a length of time is to be looked upon as an indication of organic disease. In elderly persons it is probably a sign of the existence of some of the degenerative changes described in the chapter on the heart. To make a correct prognosis in such a case it is necessary to recollect that the future depends upon the progress of the disease, for the fact that the patient continues to live shows that it must increase to cause death. The irregularity of the heart which it is intended to indicate is not the mere intermitting which is very common at almost all periods of life, but irregularity to such a degree that no three pulsations of the organ follow one another in regular and even succession of time and force. This violent irregularity may be present for as much as ten years and the patient still be living a comfortable and active life at seventy-nine years.

Having described symptoms and forms of organic disease the existence of which is not incompatible with the continuance of enjoyable health, it will be well to try to show something of the other side, and to indicate under what conditions it is likely that life cannot be greatly prolonged. This will not be easy to accomplish, but a few things can be mentioned that may generally be considered to warrant the prognosis of speedy death. It has been shown that for practical purposes it is correct to say that the direct cause of death is always to be found in the brain, the heart, or the lungs. It will be unnecessary here to say very much of prognosis in brain disease. Although there is the best reason, derived from the study of pathology, for thinking that the brain often partakes in a most important way in the wide-spread processes of chronic disease, the involvement of the brain does not generally occupy the attention very much. The reason is that if there are symptoms which distinctly denote organic brain lesion the disease is judged and the prognosis made according to such rules as exist for prognosis in brain disease. On the other hand, if the brain is involved in a latent manner as a complication of general chronic disease and death takes place owing to the brain directly, it is generally so sudden that there is no prognosis. Sudden death in most instances is unexpected death, and therefore means a total failure of prognosis. It is not intended to say that in the latter stages of chronic disease no attention should be paid to the bodily feebleness and the clouding of the intellect as indications of the approach of death, but that in most

instances they cannot be made use of to forecast the future as can be done by other means, for they generally come only toward the last, when it is evident that death is near. From the examination of the heart and lungs can be derived the most certain knowledge that chronic disease has reached the stage when the prognosis of speedy death should be made. It has been shown that prognosis based upon an estimate of the state of the kidney is very unreliable, because the most extreme degrees of fibrosis and contraction may exist and comfortable health be maintained. Although it is certain that inflammation of the kidneys may induce death, there is as yet so little definite knowledge obtainable in regard to their inflammation during life that little can be learned in that way. It is true, therefore, but the fact is not given its due weight in practice, that prognosis, even when the case is plainly one of chronic Bright's disease, should be based much more upon a study of the condition of the heart and lungs than upon anything else. It has been repeatedly stated that chronic organic disease is usually wide-spread, and therefore in prognosis each of the organs should be thought of in turn and an effort made to form an estimate of their probable condition, but no other organs so lend themselves to physical diagnosis as do the heart and lungs, which throughout life are perpetually in motion and always making sounds, while the workings of all the other organs are silent. The worst may be mentioned first. There is no chronic disease which warrants a more gloomy prognosis than that in which the heart has become very large, with a heaving impulse, perceptible over an unnaturally great area, and the lungs begin to show signs of inflammation. Correct observation of the condition of the heart and lungs and a just interpretation of the meaning of the signs yielded by their examination has long seemed to me to constitute the key to success in prognosis in chronic disease. It is not that the other organs—the liver, the kidneys, the digestive apparatus, and even the spleen—may not have a preponderating influence in causing death, but they are deeply hidden and work silently and their condition cannot be known, and finally they must work through the heart and lungs, and by the effect that is produced upon them the fatal result is brought about. It is difficult to know to what extent to dilate upon this subject, for there is so much that can be acquired only by experience, and many of the signs that indicate that disease is drawing to its end are so subtile that they can hardly be put in words. The fact that in the great majority of instances the direct cause of death is to be found in the

lungs has already been discussed (page 96), and it follows that it is most important in prognosis to attain as just an estimate as possible of their condition. It has also (Chapter VI.) been shown that the lungs are involved as often as or more often than the other organs in the fibroid processes which are common to the advance of life and to chronic disease. When in addition to these chronic lesions, which may be inferred in most instances to exist, even if the direct evidences of their presence are absent, there comes œdema of the lungs or hypostatic congestion or hypostatic pneumonia, the condition of the patient is bad, and if he does not succumb to the immediate attack he will to a subsequent one. The certainty of the recurrence of these attacks is surprising, and sooner or later one of them must prove fatal. The mode of livelihood is a most important consideration in prognosis in chronic disease, especially if it has been ascertained that the heart and lungs have become organically diseased. The fatality among the poorer classes, who must earn their livelihood by physical labor, which necessarily carries with it exposure, is exceedingly great, while, on the other hand, it is wonderful how life is prolonged among those who are surrounded by every care and who will take advice to avoid effort and exposure. The taking of cold and physical effort soon cause a recurrence of inflammatory disease in persons suffering with chronic lesions who might otherwise have escaped for a long period.

The principal purpose of this chapter is to emphasize two points: first, that it is in the lungs and heart that must be sought the key to correct prognosis in chronic disease, and, second, that heretofore the prognosis in chronic disease has been of too gloomy a character. The secret of successful prognosis is to form an opinion of the bodily condition as accurate as it is possible to obtain, and then to estimate the rate at which the disease will progress; for, no matter how incurable it may be, it must become worse than at the time of examination before death can ensue.

CHAPTER XV.

THE TREATMENT OF CHRONIC DISEASE.

In the preceding chapter it has been shown that chronic disease is often less rapidly fatal than is commonly taught, that complete recovery may take place, and even that incurable disease may cease to progress, and comfortable health continue for an indefinite period. Such being the case, it is time to take a more hopeful view of the treatment of chronic disease than at present prevails. With abundant time in which to work, it is under such circumstances, if ever, that much can be accomplished by treatment. It has been said that the treatment of typhoid fever is unsatisfactory if there is no one means which is directly applicable to its cure and reliance must be placed upon general management. Nothing could be more unreasonable than such a position, if it can be shown that death would sometimes have taken place but for the intervention of the physician. It cannot be questioned that many recover from typhoid fever with good medical advice if they are simply kept in bed and on appropriate diet, who would have died if left to their own devices, to eat improper food or starve for lack of appetite, and to drag themselves about when unfit to be anywhere but in bed. It is by such simple means as these in the first place that wonderful results may be attained in the treatment of chronic disease, and the simpler the means the greater the triumph of medicine. Although medicine would still have a field and the treatment of disease continue to be useful if there were no drugs, on the other hand, it would be both unreasonable and untrue to say that their use does not lend important help to the other means applied in treatment. While acknowledging the value of drugs, it is necessary to exercise great care not to overstate the truth, for the present is a time when superstition in medicine is rife, and unreason masquerades as truth with a boldness that was not surpassed even in the days when bleeding and antimony were the two rival specifics for the cure of all disease, and when their respective advocates quarrelled with a bitterness that is incomprehensible unless we pause to reflect coolly upon some of the follies of our own day. A medical journal—and journals reflect the opinions of the time—issues a

solemn editorial upon the use of drugs, and, after highly recommending a dozen newly invented chemicals, which have not been in existence sufficiently long for any of their properties to be known, holds gentian up to ridicule as an inert and useless substance that should be banished from the materia medica. This is unreasonable, for it is well known that dyspeptics and drunkards crave a bitter for their enfeebled stomachs, experience having taught them its benefits. Among the simple bitters none has a higher or a better deserved reputation than gentian. At the same time that simple but useful drugs are decried, many others are advertised as having specific effects for the cure of one disease or another, although it should be well known that the number of specifics is extremely limited. There are diseases for which a specific treatment exists: quinine is a specific for the treatment of malarial disease, and food for starvation; and yet all cases cannot be saved. Starvation may have gone so far that food will not save life. The condition of disease produced by starvation could not be more simple than it is, and there cannot be the slightest difference of opinion in regard to the treatment that is called for, and its general efficacy, and yet the patient must die. This seems to constitute an answer to those who say that digitalis is a useless drug because it fails to cure all cases of heart disease.

For the treatment of chronic disease there are no specifics, and, as there is such an infinite variety of forms, no two cases being exactly alike, the treatment must be equally varied. It is often very difficult to decide what treatment should be applied in cases like those described in the chapter on diagnosis, which are without definite symptoms, and yet suggest strongly that there soon will be serious disease, if it is not already in existence. Under the circumstances it sometimes seems as if Bright's disease were imminent, or there are vague "gouty tendencies," or nothing more definite can be ascertained than that the patient is no longer in a state of bodily perfection. Such a condition is so common that it must often occur in the experience of every physician. At first sight it seems almost hopeless that there can be any successful treatment, when everything is so indefinite, but reflection brings the conclusion that the situation may be less bad than if the existence of organic disease were certain, and clinical experience shows that excellent results have often been obtained when they were least expected. As no objective point can be fastened upon for treatment if everything is indefinite, it has seemed to me that every effort should be directed to change the *habit of body*. By this

is meant the routine into which the functions fall with the advance of life. Just as there are personal habits, so there are *habits of body*. It is in the middle-aged or older persons that chronic disease is most prevalent. When middle age is reached, most persons have come to live in a routine way; they eat, sleep, and work in the same way day after day, and the organs and functions go on in a circle which becomes habitual to the body. When health fails or chronic disease begins, it is plain that the imperfection arose owing to some fault in the patient's mode of living. If his life had been different perhaps he would not have been taken sick. What should be done to cure the imperfection? Change at once the habit of body which allowed it to come, and as radically as can be done without the risk of injury. It may be said in criticism that no disease has been named and no form of treatment suggested, and therefore that all this is so vague as to be worthless. If that which has been alleged in the preceding chapters is true, such is not the case, and those who have comprehended them can understand what is meant by a change of the *habit of body*. Many different means may be applied to change the habit of body, but in most instances less will be attained by drugs than by management. Most important methods of treatment are change of locality and of diet. The former is generally within the reach only of the well-to-do or rich, and should not be recommended except when the prospect of amendment or cure is sufficiently great to compensate for the inconveniences or pecuniary loss attendant upon a change of dwelling. The benefit to be derived from change of diet would be to some extent within the reach of every one, were it not that the poorer classes are generally so ignorant that they cannot be brought to understand the necessity for it, and without the willing assistance of the patient no system of diet can long be carried out. It is not the poor alone who sin in this regard, for often it is impossible to get even those of the highest intelligence and education to submit to such diet and rules of life as it may be evident would be best for them. It is very difficult to curb the appetite and to change the habits, and to attain any great and permanent results in the treatment of disease by such a method it must be pursued so long that the stock of endurance of both patient and physician often fails before the end is reached.

It is very difficult to treat this subject systematically, and therefore my discussion of it may be somewhat desultory. The range of disease included must be very great, as it has been pointed out again

and again that chronic disease is generally wide-spread in its effects, and therefore diseases usually considered to have no relations to one another are found combined. It happens, too, that a case may be observed through its entire course, and when it has ended in cure it has to be confessed that the true nature of the disease was not understood. If it is possible, however, to feel assured that the condition was so serious as to threaten life, and at the same time that the treatment pursued was instrumental in the cure, such treatment must still be looked upon as satisfactory, although so little is clear. It has been said that an important part of the treatment of chronic disease is to change the habit of body. When a man begins to fail and it is decided that it is more than the mere advance of years, that he is sick, and yet no definite disease can be found to exist, there is nothing that can be reasonably treated by drugs, for there is no indication to be met. Such a case should be treated by being sent from home for a greater or less length of time, or, if circumstances forbid this, advice should be given that will bring about a change in the mode of life at home. It is in such instances, when disease has not yet reached the stage of organic lesion, that baths and the drinking of waters and the various systems pursued at cure institutions so often prove efficacious. It was not, however, to enter into a lengthy discussion of such matters, which have been better described by others, that this chapter was written, but to record something of my personal experience in the treatment of chronic disease, and my conclusions.

Those who have seen much of chronic disease must have been impressed by the surprising prolongation of the lives of some of the patients and the complete recovery of others. In the hospitals are seen the largest number of bad cases, for there the very sick congregate, while in private practice is seen another aspect, as the patients may remain for years under observation and their antecedents be well known. Of the patients who recover it is only natural to ask what influence the treatment pursued may have had in the production of the result.

It is a common experience in hospital practice that patients are brought in who appear to be in the last stages of chronic disease and dying. It may be Bright's disease or heart disease or some other of the various complications of organic disease of important organs. A common combination is dropsy with heart disease, congestion of the lungs or slow pneumonia, albumen and casts in the

urine, and orthopnœa to the extent that the unfortunate sufferer gasps for every breath he draws. These people do not all die, although at first sight and to all except those who have had experience with them it seems that they must. In some cases there are great amelioration and a short interval of freedom from suffering, or even comfort, before death is caused by a relapse. In others the acute symptoms disappear and the patients think themselves well, especially if they belong to the ignorant classes, who are hard to convince that their health is gone. It continues, however, to be plain to the physician that there is still disease of important organs and that there will be another attack. These people go from a hospital and take up their work for a greater or less length of time, according to the degree of their bodily imperfection. Sometimes a few weeks of work bring on another attack, or it may be months or even years, but the attack must come if the physician has been correct in his diagnosis and has based the prognosis on solid reason. There is a third class of those who recover, in whom, after the acute symptoms have passed away, no indication of organic disease can be found; they sometimes go from the hospital seeming to be well, and may continue so indefinitely. There can be no reasonable doubt that many of those who recover in the hospitals would have died if they had remained in their own homes, for at home they continued to go from bad to worse, and within a short time after removal to a hospital improvement often begins. It was the treatment that produced the result, and by treatment is meant everything that was done for the patient. If the term treatment is used so comprehensively it includes many things, and in order to make treatment as good as possible it is necessary to sift out among these many things that which is beneficial from that which is useless. If examined from one point of view the ordinary treatment of chronic disease which is pursued at the present day is almost infinitely various, while from another it presents wonderful sameness. It is in regard to the use of drugs that differences of opinion exist, while as concerns general management there is a fairly satisfactory agreement. Concerning drugs the preceding statement must be qualified so far as to say that there are a few of them which have been long in use and whose beneficial effects are so generally conceded that their usefulness may be said to have passed beyond the range of dispute. The present is a time of many medicines; new chemicals are made and vegetable substances are introduced with a rapidity that is startling. One year, patients with dropsy and oppression are salivated and

sweated with jaborandi; another, fever, no matter what may be its cause, is reduced by large doses of antipyretics; a third, nitroglycerin is said to have marvellous properties in the treatment of diseases involving disturbance of the circulation, and, as the circulation is affected in almost every form of sickness, the range of the reputed field of usefulness of the drug is almost without limit. It is only a few years since the world of medicine was disturbed by a clamor that the injection of sulphuretted hydrogen gas into the rectum was beneficial in the treatment of consumption, and for a few months this absurdity was credited to such an extent that medical journals were filled with accounts of the relief and cure of consumptives by it. To any reasonable mind not preoccupied by the search for new medicines the fallacy of this restless desire for novelty is evident. More would be accomplished if the same time were devoted to trying to attain greater perfection in the management of drugs already known to be of use, for there is still room for very great improvement in this direction. It is impossible that drugs that are so lauded for a year or two and then forgotten can be of great value, and when one remembers the prostration that follows the salivation and sweating produced by jaborandi, or the equally powerful effects of other medicines that are used, there is no escape from the thought that, if no benefit is obtained, it is certain that harm is done. In regard to the use of drugs one principle has so deeply impressed itself upon me that my opinion is very fixed. It is that when the use of moderate and ordinary doses is ineffectual, large doses will generally prove equally so, if not injurious. Sometimes large doses given for a short time, to tide over an emergency, may be useful, but when they must be long continued they generally are inefficacious. The failure is for the same reason probably as that for which food will not always cure starvation, although it is the specific. The disease induced has gone so far as to be incurable. If an ordinary dose of a drug produces no good effect and a large one does no better, it by no means shows that the medicine is always useless, for the case may be one too far gone for help. The belief has been expressed that treatment of chronic disease often directly brings about a cure, and at the same time it has been shown that much of the drugging that is now in vogue is useless, if not injurious. If such be the case, it is some other portion of the treatment that brings about the result. Dropsy with oppression has been mentioned as a type of chronic disease, and patients so affected are usually kept in bed and on milk diet; the circulation is supported by

digitalis and stimulants, opium is given to soothe, the state of the functions and excretions is examined, and such medicines as may help their efficiency of action are given. This is the treatment that cures chronic disease, or, if it has passed beyond the possibility of cure, gives a temporary reprieve, or, in the worst cases, at least alleviates the suffering.

It is not desirable in a work like this to discuss at length the treatment of chronic disease, for it would necessitate the writing of a complete treatise on therapeutics. My desire is to express my disapproval of the excessive use of new drugs whose effects cannot be understood because they have not been known sufficiently long, and, on the other hand, to express my conviction of the value of that treatment of chronic disease which is based upon common sense and experience. Years of trial have brought to me the conviction that many cases that would have died without it are relieved or recover under a treatment consisting of a suitable regimen, appropriate diet, attention to the functions and secretions, and the use of medicines like digitalis, opium, stimulants, and many others. The treatment which is most successful is that which has been called symptomatic, and this is not difficult to understand when it is recollected that chronic disease is wide-spread in its effects and the lesions are often incurable, in which case the utmost that can be accomplished is to get the organism into such a condition that life may continue, and, if possible, in comfort. The treatment which will accomplish most in chronic disease has now been outlined, and the opinion that a more hopeful view of treatment should be taken, as it effects much more than the pessimistic concede, has been elaborated.

Another class of chronic disease may be formed, of cases having demonstrable disease of grave form, but as yet at an early stage. In such cases it is important to ascertain whether there is organic lesion besides that of which it is possible to be certain, and most important of all is the question what treatment should be instituted to cure, or, if cure be unattainable, to prolong life and comfort to the utmost possible. The condition it is intended to designate cannot better be made plain than by the description of a case representative of one form of it. A man about sixty years of age, who weighed a little more than two hundred pounds and whose boast was that he had never known a day's sickness, was taken with extreme irregularity of the heart. He had quite frequent attacks of vertigo, during which he never fell, although his lips were blue, and he became subject to diar-

rhœa, which was very prostrating but did not deprive him of appetite. He had lived an active life, and, having an excellent appetite, ate freely, probably largely, and of rich food, but drank almost nothing,—never taking spirits, and seldom wine, and then only in the greatest moderation. The irregularity of the heart was violent and persistent, but no other direct evidence of disease was discovered, although it may almost certainly be inferred that fibroid changes of many of the organs, especially of the kidneys, exist. At the present time, after ten or twelve years, the patient, being over seventy, is living and still in active business. During the whole of the period which has elapsed since he was taken sick the heart has always been violently irregular, although it has been less tumultuous in its action during the last year or two than previously. He has been subject to diarrhœa, and twice has had slight catarrhal pneumonia. His weight has fallen from two hundred and twenty to one hundred and eighty pounds, and he continues in perfect comfort and enjoyment of life. An outline of the case having been given, the treatment will now be described, and it does not seem possible to think otherwise than that it has had a great influence in effecting the prolongation of life. At the beginning of the illness this man was directed to avoid physical effort as much as possible, to ride whenever he could, and to walk only when he was obliged to, and then as short distances as possible and slowly. He was advised to go to his place of business only once a day, going both to and from his home in a carriage or in the public conveyance, and, after taking his mid-day meal at home, to rest or sleep and read in the afternoons, except in the summer months when driving in a carriage is agreeable. The diet was very important, and required careful regulation. It was explained to him that, as he was unfit to take exercise, a less amount of food would be required than when he had been more active. At the same time he was told that all sorts of fancy articles of food, which he was very fond of and had indulged in freely, would be injurious; that they were nearly as bad as the overuse of spirits. Pies, puddings, and cakes were all interdicted, and he was told to eat only the simpler articles of food, and that he might safely take any of these. With such a patient it is unwise to make the regulations too stringent, for if the appetite is not allowed some natural gratification life becomes so irksome that medical directions are thrown to the winds. This man was told to eat a light evening meal, consisting simply of bread and butter and tea, or occasionally, if this was so tiresome as to be unbearable, to add to it one simple dish, but

to restrain the appetite. At mid-day was taken the best meal, and at that time he was told to eat as much as he wanted, but that it should be simple and not varied beyond certain limits. The mid-day dinner has consisted of soup and a simple joint with only two vegetables, and, as an ordinary thing, no dessert. A dessert like rice-pudding might be taken occasionally when the desire for it could no longer be resisted. Breakfast was to consist of bread, coffee, eggs, and a simple dish of meat. The patient was instructed that what he needed was a reduction of the quantity of food taken, that he was to cease the use of desserts and rich dishes, and that it was exceedingly important to make the evening meal a very light one. He was told that it was not important for him to cease eating beef because mutton was less gouty, or to confine himself to poultry because red meats had some specifically bad effects.

A great deal of stress is often laid by physicians upon the evil effects of beef, which is said to be gouty. It is probable that the ill effect of meat is much exaggerated, and medical directions often fail because persons are advised to avoid eating meat when their real need is a general reduction of their daily food. If a patient is told to dine at mid-day upon soup, joint, and two vegetables, the dinner is good enough, and yet, being simple, the risk of over-eating is not very great. On the other hand, if ordered to eat no red meat, but to take in its stead only poultry and fish, persons soon become so disgusted that it is impossible to eat at all, and all advice is thrown aside. The directions, therefore, for the diet were that the breakfast and dinner should be simple, and the dinner eaten at mid-day instead of at night, and that the evening meal should be of the simplest possible nature, and very little eaten at that time. No restriction was placed upon the quantity to be eaten at breakfast and dinner, but only upon the number of dishes, and all rich and fancy food was prohibited. There is good reason, founded upon experience, for believing that the mixture of many different kinds of food at one meal has a bad effect upon the system, especially if the practice be long continued. This patient was given a prescription for ten drops of tincture of digitalis and two and a half grains of carbonate of ammonium. The medicine was taken for a good while after the commencement of the illness four times a day, and since that time, during the whole period of more than ten years, the patient seldom passes a day without it. Generally he takes two doses a day, one after breakfast and the second at bedtime, but if the heart is more irregular than usual, or he has giddiness or is weak, he

takes three or four doses, according to the circumstances. A number of times the digitalis and carbonate of ammonium were withdrawn, but on each occasion the patient was less well and their use was promptly resumed. At the present time this man enjoys very satisfactory health, the heart being less irregular than it was some years ago, although even now there never are many regular successive beats. No reasonable physician of experience can doubt that this patient has organic disease of the heart, and the inference is a fair one that the nature of this is degeneration of the muscular substance, probably of some one of the forms described in the chapter on the heart, and that there is disease of the blood-vessels. Disease of the blood-vessels is often a most important element in heart disease, and it has been shown (Figs. 4 and 5) how it may be of such a form as to cut off the supply of blood and thus starve the organ. If there is any truth, however, in what has been so often already said of the manner in which chronic disease spreads over a wide extent, and especially in the old, who are as naturally fibroid as old trees are naturally brittle, it is a matter almost of certainty that the man whose history has been described has other organic disease besides that of the heart which revealed itself by the objective sign of excessive and long-continued irregularity. Precisely what this may be is a question of diagnosis, and therefore not suitable for discussion in this chapter, it being sufficient for the present purpose to keep in mind that the disease is not confined to the heart. It will be well, before leaving the case, to dwell upon the important points of the treatment. The treatment ranges itself naturally under three heads,—regimen, diet, and medicine,—and it is difficult to say that one is more important than another, for they are essentially supporting to one another, and no one of them is capable of effecting its best results without the help of the others. Much has been written of late years in regard to the need of exercise for the cure of organic heart disease, and in some cases mountain-climbing has been recommended for this purpose. No one will question that rest in bed is an essential part of good treatment of some forms and stages of heart disease, and that in others as quiet a daily routine as possible and the avoidance of physical effort are essential. Even if it be conceded, therefore, that an active life with regular exercise is sometimes best, it is certain that at other times the greatest possible degree of quietude is essential. The conviction has long since come to me that in a case such as the one described, an old man with irregular heart and giddiness and becoming less strong, the only

wise course is to obtain for such a patient the greatest possible amount of quiet. A day or two in bed occasionally would have been very beneficial, but the patient is a very stirring man, and would fret to such a degree if kept in bed that such a course would have been impossible. The reason so much emphasis is laid upon the necessity for the advice that was given, to avoid effort so much as never to walk when it was possible to ride, is that it seems to me that it was probably more important than any other one thing in the successful management of the case. Had this patient not been warned against the dangerous effects of the active life which he loved, and which he gave up only because warned in such a way that he was convinced of the need for quiet, there can be little reasonable doubt that his struggling heart would have failed and he would have been long since dead. Quietude, therefore, was an essential of the treatment. The treatment of heart disease by exercise when it is clear that there is organic lesion of progressively degenerative nature seems to me a dangerous method and capable of doing great harm in many cases. On the other hand, well-regulated exercise for the cure of nervous disturbance of the heart is so certainly useful as to require no argument in its favor. It has already been said that cardiac murmurs indicating that injury of the valves has occurred are often unimportant, and certainly less important than disease of the heart-walls. Such murmurs result from attacks of acute inflammation, rheumatism being the type of disease which most often causes them. After an attack of acute endocardial inflammation the distortion of a valve-leaflet which produces a murmur may be almost disregarded in treatment if the walls of the heart continue sound, and exercise to any reasonable extent may be recommended. Cases of this nature are of frequent occurrence, especially among young persons, and formerly, when less well understood than at present, they were thought more serious than they are, so that those suffering with them were subjected to treatment that was unnecessary, and many useless precautions were taken. When the general condition is good no treatment is required under the circumstances. It is highly probable that it is cases of this nature that have improved under the mountain-climbing treatment. The importance of appropriate diet in a case like the one under consideration can hardly be over-estimated. Any one who has had the charge of animals knows how their condition can be changed by the quantity and nature of the food. If the appetite is good, it is generally an easy matter to make a horse or a dog fat or lean at will by the manage-

ment of the food. The patient was a man with a large appetite, and his habit had been to eat much and of rich and fattening food. It became necessary on account of his heart to stop his activity, and therefore his diet had to be made to fit the changed circumstances, besides which it was almost certain that the quantities and cloying nature of the things he had habitually eaten were in excess of what his system could dispose of and maintain itself in good condition; therefore the food had had an influence in producing disease. It was very evident that there were two important things to be done,—to reduce the quantity of food and to stop the eating of rich and unwholesome things. Being a hungry man, it could not be expected that he would at once change his habits and reduce his food beyond a certain reasonable point, therefore it was expedient to allow him to eat as much as he wished at breakfast and mid-day, and to effect the needed reduction in quantity of food by limiting the number of things to be eaten at one meal and allowing only wholesome and plainly cooked food. Not many men have so strong an appetite as to over-eat when the food is plain and the dishes are few. Experience has convinced me that persons with disease such as the patient had are greatly benefited by making the evening meal a very light one. No reason can be given for this, but it is a fact established by observation and is very important. The light evening meal will be found to be a great help toward cure, and most reasonable patients can be induced to submit to it, if only the advice given in regard to what should not be eaten at other times is not made too stringent. In recommending any system of diet it is necessary to study the character of the patient and try to estimate the degree of his self-control, making the rules elastic to suit the case, so as not to ask for an amount of self-denial of which the person is incapable. A diet may be theoretically good but practically unattainable. The eating of meat alone has been recommended for the treatment of diabetes. If there are people in the temperate regions of the world who could live for any length of time upon meat alone, they are very few, and it is not worth while to recommend it as a system, for it is impracticable.

Except for short intermissions, the patient whose case has been described has taken digitalis and carbonate of ammonium during more than ten years. Experience in the treatment of cases of heart disease has convinced me that digitalis and carbonate of ammonium, given in the doses that have been mentioned, are important adjuncts to diet and regimen. Large doses are not often prescribed, except in cases

which seem immediately to threaten life, and under such circumstances not so much is to be expected as in less severe conditions, when there is more time in which to work. Large doses generally seem less beneficial and produce less satisfactory results than moderate ones: this is pre-eminently true of digitalis. Great quantities of it may sometimes seem to help in tiding over an emergency, but when the condition appears so desperate that the physician feels impelled to continue the administration of large doses of digitalis for a long time, it soon comes about that, in studying the state of the patient, it is impossible to be sure whether some of the bad symptoms are caused by the disease or are due to the great quantities of the medicine. To illustrate what is meant: a patient under my charge with organic heart disease had been given fifteen minims of tincture of digitalis every two hours for more than a week. The amount taken daily, therefore, was three drachms of the tincture, making more than two and a half ounces in a week. Estimating that each fluidrachm of the tincture is equivalent to eight grains of powdered digitalis, twenty-four grains were taken daily, and two and four-fifths drachms of the powdered drug within one week. It is rather surprising, and contrary to much of the usual teaching, that a man could take so great an amount of digitalis and live, and the fact is worth remembering, for it makes it probable that more digitalis is required to kill than is generally supposed. The therapeutic puzzle presented by this patient at the end of the week when he came into my charge was very difficult to disentangle. The cardiac action was weak, intermitting, and irregular in the highest degree, there was constant vomiting, and the patient was bathed in cold sweat so that he appeared to be almost in collapse. Scientific therapeutists, who have studied the mode of death from poisonous doses of digitalis, say that as the poisoning goes on the heart contracts more and more firmly, then the muscular spasm becomes so great that the ventricles no longer dilate fully during diastole. The ventricles dilate less and less, and finally death takes place with the heart tightly contracted and almost empty of blood. Pathologists know that in cases like that described, in which the heart is generally large and heavy and the walls organically degenerated, it is common to find after death that the heart is fully open, all the cavities being distended to their greatest capacity with blood which is more or less clotted. It is easy to draw the conclusion that for some time before death under these circumstances exactly the opposite of what happens in digitalis poisoning obtains: the heart is filled with blood, some of

which is already clotted, and the muscular action is feeble, so that at each contraction only a little blood is expelled and none of the cavities are ever emptied. Which of these states of the heart and circulation existed in the man who had taken large doses of digitalis for a week, and what treatment did he require? As there has never been much opportunity to watch how death would take place if a man with an enlarged and degenerated heart were poisoned with digitalis, most of what is known of the mechanism of digitalis poisoning having been learned from the observation of it in animals with healthy hearts, it is impossible to know what effect the drug does produce upon a heart diseased like that of the man whose condition has been described. For the clinician there was only one reasonable conclusion: the patient had had digitalis enough. The large quantity taken had failed to do any good, and if the use of any digitalis had been continued it would have been impossible to be certain that the bad symptoms were not partly due to digitalis poisoning. It was directed that the patient should lie as still as possible, and should take every two hours an ounce and a half of milk, with half an ounce of lime water and two fluidrachms of brandy. A quarter of an hour later was given one-sixteenth of a grain of sulphate of morphine, with two minims of chloroform, and a teaspoonful of compound tincture of cardamom, in a little water. All other medicine and food were forbidden, and instructions were given that the greatest regularity was to be observed in the administration of the liquid nourishment and medicine, that they were to be given regardless of whether the patient vomited immediately before or after them, and that nothing else was to be tried for some time, even if the vomiting continued to such a degree that it seemed as if everything taken into the stomach was ejected. In the course of a day or two the vomiting and cold sweating ceased, but the heart continued to be irregular, although it improved in strength. It was many weeks before the patient gathered strength enough to be able to sit up, but finally he was discharged from the hospital in a comfortable condition, although still suffering with heart disease to such a degree that it seemed unlikely he could live very long. The history has been narrated to show how ineffectual even the largest doses of digitalis proved in a case in which recovery from the acute attack took place under the use of soothing and mildly stimulating medicines, careful regulation of the food, and profound rest. It is instructive also to notice how the difficulty of attaining a correct judgment of the case was made greater because of the prob-

ability that the symptoms were partly due to poisoning by the medicine, and the impossibility of distinguishing what might be the symptoms of poisoning from the symptoms of the disease. It illustrates how large doses of medicine may fail to benefit or may even do harm, just as the case of long-standing irregularity of the heart in an old man illustrates the usefulness of small doses of digitalis continued for a long period. This leads to an important question: How much digitalis can with advantage and safety be continued for a long time? The result of my reading and experience has been the formation of the opinion that ten drops of tincture of digitalis may be given three times a day as long as may seem desirable, even for a year or more, but not more than this dose unless the patient is kept constantly under medical supervision, so that it may be stopped if desirable. This statement may seem somewhat dogmatic, but it is necessary to set dogmatic standards in dosage, and the amount named will be found a fitting one in cases in which there is no idiosyncrasy. In connection with what has been related of the patient to whom large doses of digitalis had been ineffectually given it may be well to dwell upon the good results that were obtained from opium, and to say how very useful it often is in cases of chronic disease in which there is pain or great nervous disturbance of almost any kind. This is especially true of heart disease. If there is vomiting in addition to the other sufferings common in heart disease, the use every two hours of one-sixteenth of a grain of sulphate of morphine, and two minims of chloroform, in a teaspoonful of compound tincture of cardamom or other aromatic containing alcohol enough to dissolve the chloroform, is often most efficacious. Doses as large as these must of course be given only so long as the patient is under constant supervision, and generally should not be continued beyond a week or two. The doses of opium and how it should be used in disease are not fixed in text-books in such a way as to make it easy for one seeking information to understand. For instance, the United States Dispensatory (edition of 1883, page 1076), in advising in regard to the dose of opium, mentions that as little as one-fourth or one-third of a grain is sometimes given, and then adds, "in acute peritonitis we have seen the equivalent of seventy-five grains given during the twenty-four hours with advantage." Finally, it says, "The ordinary dose of dried or powdered opium may be set down as one grain." The advisability of ever giving as much as seventy-five grains of opium in twenty-four hours is a matter in regard to which physicians would

greatly differ, while the other doses mentioned are beyond question such as are usually fitting and beneficial. The advice, however, is insufficient, for it is not stated how much should be given in cases of chronic disease or in other conditions in which it is deemed that benefit would accrue from its soothing or supporting or other effect. It is very desirable that clinicians should have some fixed standard of dosage of opium parallel with that which has been fixed for digitalis. It ought to be generally known how much may be given continuously for several weeks without passing what is called by therapeutists the physiological limit and producing poisonous effects. Having carefully studied this matter and having often watched the effects of the quantities to be named, I feel warranted in stating that the ordinary human adult can take one-quarter of a grain of powdered opium, or ten drops of laudanum, every two hours for several weeks successively, and there will be no contraction of the pupils, no unusual sleepiness, nor any other symptom of the narcotic effects of the drug. These doses equal three grains in each twenty-four hours, or, if laudanum be used, four grains, if the estimate is correct that thirty drops of laudanum equal one grain of powdered opium. What would be the effect of this amount of opium upon a person in good health it is impossible to state, for physicians do not have occasion to give opium to any but persons suffering with disease. The doses named have a very decided effect in quieting pain, if it be not too severe, and, as has been said, no symptoms whatever of the narcotic effects are produced. It is certainly desirable to have some standard of dose which shall be precise in regard both to the amount to be given at a time and to the intervals between the doses. It may be given in the manner that has been described without danger in all forms of chronic or acute disease in which its effects appear likely to be useful, unless there is evident reason to the contrary.

There have now been mentioned three stages of chronic disease, and the treatment of each of them has been discussed. These stages are, first, that in which disease has progressed to an extreme limit, it being evident that important organs are organically changed and life threatened with immediate extinction. As a type of this was mentioned the condition which is so commonly seen in hospital practice in which dropsy and oppression are the prominent symptoms. The second stage is that form of disease in which there is distinct evidence of organic lesion but life is not immediately threatened, although it is plain that death must be the consequence of a

great increase of the disease. As a type of this stage was given the account of a man sixty years old with intermitting heart. The third stage is that form of disease in which the symptoms are very vague, it seeming as if organic lesion must be already existent, although no subjective evidence of it can be discovered, or that organic lesion soon will arise if the bad symptoms continue. It was said that for this stage of chronic disease it is essential to endeavor to change the *habit of body*, especially as under the circumstances there is no indication for any more direct treatment or for medication. The management of this last stage was less fully elaborated than that of the other two, and it will be best, therefore, before closing the subject of treatment, to make some further statements in regard to it. Chronic disease should be more susceptible to the influence of good management at its beginning than when more advanced, for the less the organic change the more likely is it that a perfect cure can be effected, and if there is no organic lesion it is required only to effect a cessation of the disordered state of the organism to attain a cure. The advantages of change of climate were mentioned, but as that most valuable means of treatment is a special subject it would be inadvisable to attempt its elaboration here. It was also said that cure institutions and mineral springs, where special systems of living have been arranged, are often most efficacious methods of changing the habit of body. These systems of treatment have been brought to much greater perfection in Europe than anywhere in America, although there is reason to think there are natural mineral springs in this country which are equal to any to be found elsewhere. Springs, however, have comparatively little value unless their properties have been long studied and a system of life instituted at them which places those who seek treatment under the care of experienced physicians.

In connection with the subject of the treatment of chronic disease while still in its earliest stage, there may be mentioned a condition which is very common in civilized life, and which, if the truth be told, is even yet but little understood, although it has engrossed a large share of the attention of physicians. It is that state of disease or disorder in which an excess of uric acid is found in the urine. Most commonly uric acid is discovered in the urine of persons who have consulted a physician because of headache or digestive disorder, or perhaps only of vague malaise without special symptom of any kind. The physiology of this curious condition is not understood, but its concurrence with disordered digestion has been so frequently observed

that it is almost certain that the two are related. The clinical observation has often been made that uric acid will disappear from the urine, and all the uncomfortable symptoms that commonly accompany it disappear also, when the patient has the amount of his food reduced, if he is taking too much, or his manner of living regulated. Uric acid lithiasis often disappears completely, and the individual who has been affected with it seems as well as before the attack. On the other hand, it is not infrequently the precursor of chronic organic disease, and therefore it is important in all cases to endeavor to institute such treatment as will cure it, which will be most certainly accomplished in the majority of cases by trying to change the *habit of body*.

A valuable means for accomplishing a change of the habit of body is the use of milk diet. Patients who for any reason cannot have change of climate may often find milk diet a good substitute. In any of the vague forms of chronic disease that have been discussed in which the existence of organic disease is feared, or in which it is thought it will come if not prevented, and no indications show that some particular treatment or any special medicine is called for, milk diet may be used. It is often very difficult to get middle-aged or older persons to change their habits, and frequently such people cannot go to a European spring or have a temporary change of climate. Such persons can be put upon an exclusively milk diet for six weeks and still continue their ordinary vocations, unless their mode of life be an unusually active one. The quantity of milk necessary to be taken daily is from two and a half to six pints; delicate persons and women often do best with the smaller quantity. If two and a half pints are ordered, half a pint may be taken at eight and eleven in the morning, and at one, four, and seven after noon. In taking two quarts the patient should be given half a pint every two hours, beginning at eight in the morning and continuing until ten at night. It is important to fix the amount, and the hours when it is to be taken, for if this is left to the individual too much or too little will almost always be taken. Patients put upon milk diet as a means of treatment in the manner described should be kept to it rigidly for six weeks, and then gradually go back to the use of ordinary food. Persons upon milk diet can, as has been said, generally continue their vocations, and the change of the bodily condition that is effected by such a revolution in regard to food is wonderful. The change alone is frequently very beneficial to the health, although, of course, if the patient, as soon as the six weeks have passed, lapses from the milk diet to his old habits,

only temporary improvement can be expected if the disease was of serious nature. Another gain, however, is often derived from milk diet, which is that after a patient has for a period of six weeks lived upon milk alone his ordinary ways of life as well as his habits of body have been so thoroughly revolutionized that it is generally less difficult to get him to submit to the rules of regimen, diet, and medication that seem best. Only those who have practised medicine can appreciate how difficult it is to get patients to submit to the simplest and most palpably necessary rules of life. The things they are told to do seem so simple that they cannot be brought to believe them of sufficient importance to take the trouble to remember them and to carry out what they are told must be done. A man, however, who has been for six weeks upon milk diet is like a field which has been ploughed and lies fallow for the seed. He does not know exactly what to eat, and he is ready to be directed. The directions given at such a time are likely to be carried out for a good while with much regularity, although, of course, if a watch is not kept the patient will probably fall back into his old habits. Milk diet has been highly recommended and much used for hysterical women, but not so much for men and for organic disease in the manner that has been described. It must not be thought for that reason that it is not a powerful means to affect the health, for it can be beneficial, when correctly used, for men who have been robust as well as for women. Thus milk diet may accomplish two important things: it often, unaided, brings about the desired change of the habit of body; and it gives an opportunity to institute such rules of living as seem necessary by bringing the patient into a condition of submission, so that he will heed advice.

In the chapters dealing with the various organs it was shown that in chronic disease the commonest pathological lesions are fibroid growth and disease of the blood-vessels, and emphasis was laid upon the fact that these conditions render tissues so changed specially liable to inflammation. Inflammation, therefore, which is frequently of latent character, is almost an essential part of the ordinary processes of chronic disease. In dealing with questions of treatment it is very important to keep this fact in mind. There cannot be two opinions in regard to the value of rest in the treatment of most forms of inflammation. Whenever in chronic disease there is inflammation, or even strong reason to suspect its presence, it is in most instances good treatment to endeavor to keep the part quiet that is inflamed, or, if

the condition is a general one, to procure rest for the individual, and this can generally be accomplished by putting him to bed. The duration of the rest must, of course, be determined according to circumstances. The importance of rest in the treatment of chronic disease could hardly be exaggerated. Those who are chronically ill are often allowed to drag themselves about, becoming all the time worse, when so simple a measure as going to bed for a few days would turn the tide so as to make it set in the direction of cure. It may be laid down as a rule that during the periods when there is inflammation in chronic disease rest is indicated.

It could hardly be expected that after having spent a large part of my professional life in clinical work I should have resisted the inclination to write upon treatment, for it is the most important of all subjects in medicine, and no one can practise profitably without forming opinions. That which has been expressed has been of necessity somewhat desultory, for it consists only of my own views and impressions and has been written without any wish to make a complete treatise upon any of the subjects discussed. This has not been because I have not formed definite opinions upon many and important points in regard to the treatment of chronic disease. The principal of these points are, first, that the treatment of chronic disease should be approached more hopefully and with greater confidence than is usual, because so much can be accomplished for its cure, or, if that be impossible, for its relief. Secondly, too many drugs should not be used, as it is reasonable to suppose that the number of them that are of real value is limited. On the other hand, it is certain that the few drugs whose beneficial effects have been established are essential to enable any one to accomplish the best results. Thirdly, there is no specific treatment for chronic disease, but it must be managed by common-sense rules, and the best form of treatment is that which has been called symptomatic. As yet there are few systems of treatment, but more must soon be established, and meanwhile the cases which are vague and without anything to show that some particular treatment is required are best managed by trying to effect that which has been described as a *change of the habit of body*.

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