A STUDY

OF THE

HUMAN BLOOD-VESSELS

IN HEALTH AND DISEASE

A SUPPLEMENT TO

"THE ORIGIN OF DISEASE"

BY

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WITH ONE HUNDRED AND THREE ORIGINAL ILLUSTRATIONS

PHILADELPHIA & LONDON

J. B. LIPPINCOTT COMPANY

PREFACE

In the latter part of the year 1899 a fire destroyed every unsold copy of my book on "The Origin of Disease." The publisher soon afterwards asked if I would not seize the opportunity to turn a pecuniary loss into an advantage by issuing a new and perfected edition. This obliged me to make an examination of my work, and I reached the conclusion that one of the best parts of it was the chapter on the blood-vessels, and that it was also the most imperfect and incomplete. When I studied the subject-matter, the origin of disease, and the secondary subject, the disease of age, I found I could not add much to what had already been set forth, but that my descriptions of the anatomy and pathology of the blood-vessels were inadequate and, besides, in the interval since the book was issued I had accumulated new facts. These facts, however, were not suitable to be incorporated with the material treated under the old title. Although the various subjects discussed in "The Origin of Disease" are intimately related, and although the new material collected had grown from the pursuit of the same studies that led to the writing of my book, it seemed impossible to weave the new material and the old together in such a way as to form a harmonious whole. It is not my intention to claim that my book on "The Origin of Disease" is complete, but, whether one agrees with my conclusions or not, there cannot be much doubt that my observations of nature are accurate. The addition of an elaborate discussion on the anatomy and pathology of the blood-vessels would have added nothing to its completeness and would at the same time have buried the added information. For these reasons I was convinced that it would be inexpedient to issue a new edition, that I was prepared to write upon the subject of the human blood-vessels, and that the discussion of them must not be confined to their pathology but must include also a consideration of their anatomy. This work is the outcome of the conclusion, and it is to be looked upon as a supplement to my book on "The Origin of Disease."

Almost all of the blood-vessels from which my illustrations were made, and upon the appearances and conditions of which my work

is based, were obtained in the course of my service as physician to the Pennsylvania Hospital. During the time that I was collecting this material the hospital organization was such that I myself made most of the autopsies or was present when they were made. Every physician to the hospital was his own pathologist, for there was then no organized department of pathology. Although there cannot be any doubt that the modern method of the division of labor is a great advance, it is certainly true that when one man was able personally to make the diagnosis and direct the treatment, and afterwards, if the patient died, to make the autopsy and examine with the microscope portions of the tissues, the opportunity was afforded to learn some things that are likely to be overlooked when the work is subdivided.

The illustrations are original; the camera lucida was used in making all of them, and the steel etchings were drawn directly upon the metal without the use of an intermediate sketch. The artists exercised their best skill and have succeeded in producing faithful representations of nature. I learned in the course of my work not to give them much advice or detailed directions. Many of the illustrations in medical books are no more than diagrams, and this I think is because the artists are too much restricted in drawing objects that they themselves sometimes feel they do not understand. As they are not given sufficient scope, they fail to reproduce that which they see, as they must all try to do in portrait or landscape work. Mr. Hermann Faber made the etchings and the pictures in color, and the black and white illustrations reproduced by photographic process are by Mr. Erwin F. Faber.

December 1, 1906.

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INTRODUCTION

It has so long been known that the blood-vessels are a very important part of man's economy that it is not necessary to apologize for the publication of anything that will add to the sum of knowledge concerning them. Human blood-vessels have not been exhaustively studied and there are no existing text-books which contain full and satisfactory information in regard either to their anatomy or to their diseases. This book is necessarily incomplete because it is only a record of my studies. It has been impossible to arrange my material as methodically as I should like, because the foundation of the work is the illustrations, and these were made from tissues that were all obtained post mortem except a few which were removed by operation from living persons. As the vessels, whether procured from the dead or from the living, had to be taken as they were found, they are grouped in the pictures according to the positions they occupied in the tissues. Hence it has been found impracticable to produce a systematic text-book, for in such works the arteries, veins, and capillaries and their various diseases are usually described in separate chapters, which are arranged in the order deemed by the author best fitted to produce a comprehensive whole that can be easily understood. My own descriptions have been written in the way the pictures have indicated to be the natural one according to the grouping of the blood-vessels and to the conditions of disease.

It is impossible to study disease of the blood-vessels without soon learning that their anatomy is still imperfectly known. The correctness of this statement will be readily accepted by any one who has, for instance, examined with the microscope the capillaries of the various organs and has tried to obtain an exact understanding of their course and appearances and who has then read such descriptions of them as can be found. Within a few years I have myself pointed out the fact that the muscular fibres of the human heart are not merely surrounded by nets of capillaries, as was believed, but that they are penetrated by the capillaries, and, besides, that the return vessels accompanying the minute arterioles of the heart frequently are not

veins with three coats, but are large capillaries with walls formed of endothelium.[1] There are so many of these large capillaries in the heart, their size is so great, and the shapes and appearances of some of them are so different (see Chapter VIII.) from ordinary minute capillaries that it would be more accurate if some of the larger ones were named sinuses. In the course of this work I shall demonstrate with pictures that the same anatomical peculiarity, of arterioles having capillaries as their accompanying return vessels, exists in the brain and in the spinal cord. Something of this is known and is mentioned in text-books,[2] but it has been by no means fully elaborated and has not yet become a matter of common knowledge. The ordinarily accepted descriptions of veins is that they are like arteries in their main features, having three coats, intima, muscularis, and adventitia, and that these three coats are of different thicknesses in the two sorts of vessels rather than that veins and arteries are of essentially different structure and appearance. Although it is certainly true that there are points of marked similarity, I think I shall be able to show that veins are more radically different from arteries than the commonly accepted descriptions indicate.

There is still much to be learned about arteries, but it is beyond doubt true that their appearances and characteristics have been more fully and accurately described than have those of veins or capillaries. The differentiation of the walls of the arteries into three separate coats which can be easily seen with the microscope, and which are essentially different from one another, is generally marked, while in veins it is often obscure or indistinguishable. Although the available information in regard to the anatomy of the blood-vessels is still so incomplete, it would never do to wait for it to become complete before studying their diseases. Anatomy and pathology must progress hand in hand, and every addition made to the one science is sure to help the other. At the present time it is not possible for one wishing to study disease of blood-vessels to obtain from books an exact idea

[1] 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.

[2] Normal Histology, by George A. Piersol: J. B. Lippincott Co., Philadelphia, 1900.

of their normal appearances. For instance, in order to study disease of the radial artery—a vessel which occupies a large share of the attention of physicians, owing to the custom of feeling the pulse at the wrist—it ought to be a simple matter to turn to works on anatomy and learn what are the gross and microscopical appearances of this vessel. Text-books of anatomy and histology, however, fail to yield such information. They are in some respects most complete, and the number of facts that have been accumulated and recorded in regard to the blood-vessels is enormous; but the information is general, and when one comes to consider particular vessels, or to study special points, it is necessary to return to the direct observation of nature. The obstacles to a satisfactory study of human blood-vessels are almost innumerable, and the amount of time that might be expended upon it is without limit.

In the study of human histology it is difficult to obtain healthy tissues, and in the text-books many of the illustrations and descriptions are of the tissues of the lower animals. This is unsatisfactory, because it is never possible to be sure that such tissues are exactly like the corresponding human tissues.

Another obstruction to the increase of knowledge of the anatomy and pathology of the blood-vessels is that little or no attention is paid to the fact that they change as life progresses, so that the blood-vessels of the old are very different from those of young persons. Whether this change be looked upon as a physiological one, as it has been considered by many to be, or it be conceded that there is a "disease of age," as I myself think and have tried to prove,[1] there can be no reasonable doubt that the difference is a real one. It is necessary, therefore, in order to make any further progress, that it be recognized that the blood-vessels slowly and steadily change from youth to age. At present it is often difficult, and sometimes impossible, to decide whether a particular vessel is diseased or if it has lost the characteristics commonly attributed to vessels of its class owing to the changes due to age. All intelligent physicians are forced to answer questions in pathology, and the difficulty that confronts the practical physician when he tries to answer the question whether a particular blood-vessel of an elderly or old person is diseased, and for

[1] The Origin of Disease, by Arthur V. Meigs, Chapter II.: J. B. Lippincott Co., Philadelphia, 1899.

that reason incapable of properly performing its function, or whether it is thick and stiff owing simply to the physiological changes of age, is one that presents itself almost every day and is often entirely unanswerable. There is no standard to establish what is a normal blood-vessel, and it is actually the case that for one wishing to study disease of such a blood-vessel as the radial artery it is impossible to know where to turn to find an accurate description and pictures of it. It is almost unnecessary to say that it would be a great help to the study of disease of blood-vessels were it possible to obtain more complete and accurate descriptions of their normal appearances.

HUMAN BLOOD-VESSELS

CHAPTER I

Arteries and Veins

The generally accepted descriptions of the histology of arteries and veins are not perfectly exact, for they give the impression that the two kinds of blood-vessels are more nearly alike than is actually the case. It is true that both arteries and veins have three coats and are composed of the same kinds of tissues and that the same sorts of cells exist in both, but the veins are more variable in structure. The walls of the veins are thinner and their texture is looser than that of arteries. They are less satisfactory objects to examine with the microscope by the methods of preparation in use at the present time. It is said that the external coat of some veins contains muscular tissue and in some veins muscular tissue is scant or is even entirely absent. In my own studies of human veins I cannot remember ever having been able to distinguish a fenestrated elastic layer, although the fenestrated or plicated membrane constitutes such a striking feature in the great majority of arteries. On the other hand, the arteries are regularly formed of three coats, and these coats are of much more definite structure than those composing the walls of veins. A great part of the common descriptions of arteries and veins has been gradually built up from studies of embryology and of the tissues of lower animals. It will be found that the human tissues which become available for examination do not present appearances in all respects in accord with the descriptions. In my experience it is exceptional to find the arteries and veins lined with the fine layer of endothelium which according to the classical descriptions always exists. Histologists say this is owing to post-mortem changes and to the imperfect opportunities for the preservation of human tissues. This seems to me a very inadequate explanation, and I believe that with the passing of years the blood-vessels and particularly the arteries change much more than has been generally appreciated. A usual result is that the intima is a tissue of irregular thickness at different parts of its circumference.

This condition of the intima of arteries, which, when fully developed, constitutes the disease endarteritis, is so universal that it is impossible to look upon it as being always a disease. In its lesser forms of development it is quite harmless, and should be set down as a departure from the standard of normal which invariably comes with the passage of time, and it must not be called a part of the "disease of age," which in its more fully developed states is a positive disease and is easy to recognize. This irregular but almost universal thickening of the intima of medium-sized human arteries is accompanied by an absence of the lining layer of endothelium. In some arteries[1] the endothelial lining can be distinguished at parts of the circumference of the vessel and at others the intima may be seen to be thickened. The tissues of the lower animals have been too much used for making the illustrations of the standards of histology, and an ideal has been set up which is too rigid. Sufficient allowance has not been made for natural variations. The illustrations in text-books are generally too diagrammatic. The custom of describing arteries and veins as consisting of three coats is so firmly fixed that it would be difficult to change it, and it is doubtful if anything would be gained were it changed, although it would probably be more true to nature to say they have only two coats. It is impossible to make any distinction between perivascular connective tissue and the adventitia of arteries and veins. The thickness of the external coat depends upon how much tissue was dragged out with the blood-vessel if it has been pulled out of the surrounding tissue and is examined separately, or it depends upon the opinion of the anatomist if a section of a vessel is examined which is still surrounded by tissue. The muscularis and the intima are the only tissues of arteries and veins which are heterogeneous to the organs or tissues in which the blood-vessels lie. The adventitia is fibrous tissue and is like much of the connective tissue of the body. It would therefore probably be more logical and more nearly scientifically correct were two coats only attributed to the arteries and veins and the adventitia classed as a part of the perivascular connective tissue.

The living blood-vessels are very different from dead ones, which are almost our only material for study. In studying blood-vessels this fact should never be forgotten, and it is just as true of their anat-

[1] Origin of Disease, by Arthur V. Meigs, page 43, Fig. 8: J. B. Lippincott Co., Philadelphia, 1899.

omy as it is of their pathology. One of the mysteries of life and death is the disappearance at death of the liquid blood that distends the vascular channels during life. The relaxed and flaccid or empty blood-vessels found in the dead are very different from the elastic and pulsating tubes that are seen by surgeons during operations and by experimenters upon living animals. Most of the investigations both in anatomy and pathology are made with dead tissues, and in studying blood-vessels allowance must always be made for the changes that take place at the time of death and afterwards. I say at the time of death and afterwards advisedly, for, although it is almost universally known that the dead tissues are different from the living ones, it is not so well known, or at any rate it has not been so much emphasized and made a matter of common knowledge, that the dead tissues which are studied have undergone a further great change in the course of their preparation for investigation.

It is to microscopical study that I now especially refer. Tissues which are to be examined with the microscope are generally subjected to processes which are more or less elaborate. Some of the lower animals have transparent tissues, and these when sufficiently thin can be examined with the microscope while still living, and in this way has been obtained some of the most valuable information in regard to anatomy and physiology. Teased bits of the tissues of recently killed animals and of criminals that have been executed have been used for study, and such tissue probably has undergone a minimum of change after death. Frozen sections obtained under proper precautions are also of use and have done their part in advancing the sciences of anatomy and pathology. All the more elaborate methods, however, used in making permanent preparations for microscopical examination involve the immersion of the tissues in various reagents, and no one of these methods is free from the objection that the tissue is very much shrunk. This shrinkage must necessarily change the general appearance of the tissue as well as the shapes and appearance of the cells and the other elements of which tissues are composed.

After trying for a good while to discover a method to eliminate this source of error, it struck me that in dealing with blood-vessels something might be accomplished in that direction by placing a rod of some rigid material, like glass, within the calibre of a vessel to

be examined with the microscope. This experiment I have tried.[1] Rods of glass were placed as soon as possible after death in blood-vessels to be examined, and then the tissue together with the glass was put in whatever reagents were needed. The glass prevents any reduction in size of the calibre of the vessel. This does not prevent the shrinkage that takes place in arteries and veins at the time of death when their fluid contents leave them, but it entirely prevents the further reduction of their lumina which ordinarily occurs in preparation for section for microscopical examination.

The sections I have had made were subjected to the paraffin-embedding process. The glass rods used were as large as could be got into the vessels without stretching them, and the glass was left in them while they were in the various reagents and while they were soaking in the warm melted paraffin with which the tissue must be permeated. The permeation with paraffin is the last stage of the process, and the glass was not taken out of the vessels until they were removed from the oven ready for the paraffin to be cooled and sections cut. There was no opportunity, therefore, anywhere in the course of the process for the calibre to shrink. When preparing sections in this way I have always kept a second piece of the artery or vein that was being studied, and have carried it through the same process of preparation and at the same time. Thus there was always a section of a vessel which had had a glass rod in it to prevent shrinkage, and another section which had been left free to shrink as it might and to assume whatever irregular shape the shrinkage tended to give it.

The examination of sections thus prepared gives ocular demonstration of a number of things that were already known by inference but which lacked direct proof. A section of any vessel which has had glass in it while in course of preparation for cutting always remains of the same shape as the glass body, and I have generally used circular rods or hollow cylinders, but other sections of the same vessel prepared without anything in its calibre are often irregular in outline. This irregularity is very variable and is due to a number of

[1] Transactions of the Pathological Society of Philadelphia, 1901. A Demonstration of the Shrinking of Blood-vessels that occurs as they are ordinarily prepared for Microscopic Examination, and of the Distortion of the Tissues which is caused by this Shrinkage: Also the Exhibition of New Blood-vessels in the Inner Layers of Diseased Veins. By Arthur V. Meigs.

causes. Large vessels generally, and veins in particular because their walls are thin, almost always collapse and assume irregular outlines; they seldom preserve their natural circular shape. The smaller vessels, and especially those with walls that have been thickened by disease, usually retain their natural circular form.

The irregularity of shape of blood-vessels cut for examination with the microscope, however, is not due alone to their collapsing because their walls were not thick enough to retain their form, but also to the shrinking of the tissue in accordance with variations of the thickness of the vessel-walls at different parts. This variation of thickness at different places occurs even in healthy vessels and to a still greater extent as a result of disease. It is also true that different kinds of tissue shrink very differently when they are soaked in the various reagents used in preparing sections. The adventitia of the aorta, for instance, which is of loose and open structure, will shrink more than the intima, which is denser. This is easily demonstrated by preparing a small square section of the whole thickness of the human aorta. Soon after it is placed in the preservative fluid it bends itself backwards, the intima forming the outer and longer curve, while the adventitia forms the shorter arc. Sections of blood-vessels are often wavy, more or less irregular circles, or the vessels may collapse in such a way that the sections are without any regularity of form. In text-books of histology blood-vessels are generally described as cylindrical, but in truth it is the exception when sections of them are circular. If they have not collapsed owing to their walls being too thin to retain their cylindrical shape, the changes that occur with the advance of years cause the walls to be of uneven thickness, and then irregular shrinkage in course of preparation for section inevitably destroys the circular form. Disease, if it be present, may produce an infinite variety of unexpected appearances.

The plicated membrane, or fenestrated membrane of Henle, as it is also called, is an important anatomical landmark in arteries, and it is reputed to be often the seat of origin of disease. In the microscopical study of arteries this membrane is a striking feature, constituting as it does the line of separation of the intima from the muscularis. It is named the plicated membrane because it ordinarily appears as a wavy or folded line when seen in sections of arteries. Histologists know, of course, that the folding is due to post-mortem

shrinking and that during life the membrane is a cylindrical layer of elastic tissue. Two sections prepared as I have described, one with glass in its calibre and the other without, show very clearly this peculiarity of the plicated membrane. The sections which have had no glass in their lumina are generally irregular in outline instead of being perfectly circular, and are much smaller.

Figs. 1, 2, 3, 4, 5, 6, 7, and 8, which show blood-vessels that were treated by the method described, demonstrate in the most satisfactory manner both the irregularity of outline of the vessels that were allowed unimpeded to shrink, and that this shrinkage is usually such as to cause a very great reduction in the size of the calibre. Fig. 1 shows the aorta. One of the sections was allowed to shrink and the other was prepared with glass cylinders in its calibre. The shrunken section is of an irregular oval shape and its wall is about twice as thick as that of the other section. The odd shape of the unshrunk section is due to the fact that, as I had no glass cylinder of such a size as exactly to fit the opening, it became necessary to place one large glass tube and other smaller ones inside the artery to fill it. Fig. 2 represents the vena cava. The opening of the unshrunk section must be three or even four times as large as that of the shrunk one, and its wall is much thinner but of extremely irregular thickness. On the right-hand side of the picture the wall is fully three times thicker than it is on the left. The irregularly twisted and folded shape of the shrunk section is due to the effect of the preservative fluids upon the vein, which is of looser texture and softer than arterial tissue. It is very different from that of the aorta (Fig. 1). Figs. 3 and 4 show shrunk and unshrunk sections of the femoral artery. The great difference of the size of the openings, and the fact that the wall is very much thicker in the section in which the shrinkage was allowed to go on unimpeded, are graphically shown. Although the sections are enlarged only eight times, the three coats of which the vessel-walls are formed can be easily distinguished, and they are even more distinct in the shrunk than in the unshrunk section.

Figs. 5 and 6 illustrate the femoral vein shrunk and unshrunk. Their appearances are so different that it is difficult to believe that they are pictures of the same vessel. The wall of the shrunk section is very much thicker than that of the unshrunk one and it is folded Although the enlargement is the same as that of the femoral artery

FIG. 1.—AORTA; SHRUNKEN AND UNSHRUNKEN. (ACTUAL SIZE.)

From a man of thirty-three years who died of pulmonary congestion. The section to the left had glass tubes placed in its lumen at the time the post-mortem was made; both it and the section represented by the picture to the right were then preserved in alcohol. The amount of shrinkage is easily seen, and it is also evident that the wall of the shrunken vessel is thicker than that of the unshrunken one. A number of the following figures are from the same case.

FIG. 2.—VENA CAVA; SHRUNKEN AND UNSHRUNKEN. (ACTUAL SIZE.)

From the same case as Fig. 1. To the right the shrunken, to the left the unshrunken section. The lumen of the shrunken section is much smaller than that of the other one and its wall is thickened and is folded. The wall of the unshrunken section is of very varying thickness at different parts. It might have been anticipated that the loose texture and thin wall of a vein would shrink and become distorted more than the firmer and stiffer artery. *t*, a region represented more highly magnified by Fig. 16.

FIG. 1.

FIG. 2.

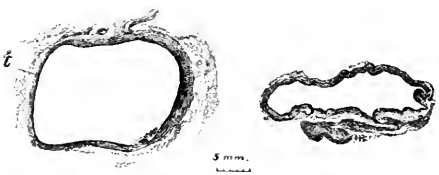


FIG. 3.—FEMORAL ARTERY; UNSHRUNKEN. (× 8.)

From the same case as Fig. 1. Shrinkage was prevented by a glass rod. The contrast with Fig. 4 is striking, for the lumen is very much larger and the wall much thinner.

FIG. 4.—FEMORAL ARTERY; SHRUNKEN. (× 8.)

From the same case as Fig. 1. The usual shrinkage was allowed to occur. The contrast is great, for the calibre is small and the vessel wall thick and somewhat corrugated upon the edges from the drawing together of the tissue.

FIG. 3.

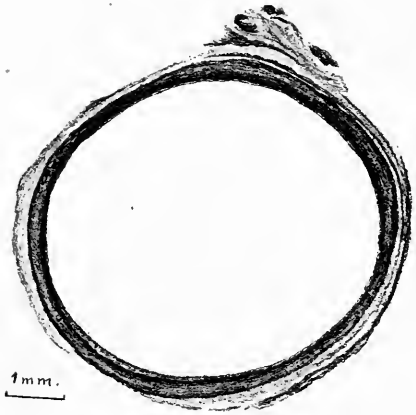


FIG. 4.

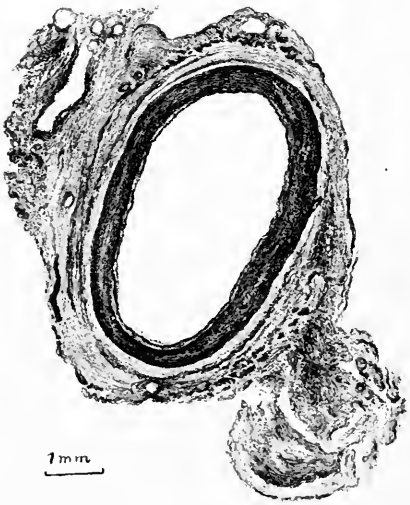


FIG. 5.—FEMORAL VEIN; UNSHRUNKEN. (× 8.)

From the same case as Fig. 1. The lumen of the vein is large and it is circular. The wall is of very varying thickness at different parts of the circle. The outer part of the wall below and to the left contains many bundles of tissue which run in the direction of the length of the vein. When examined with higher power these appear to be involuntary muscle. No such muscular layer is represented in the pictures showing the ordinary histological condition of veins. The portion of vein shown was prepared with a glass tube in it.

FIG. 5.

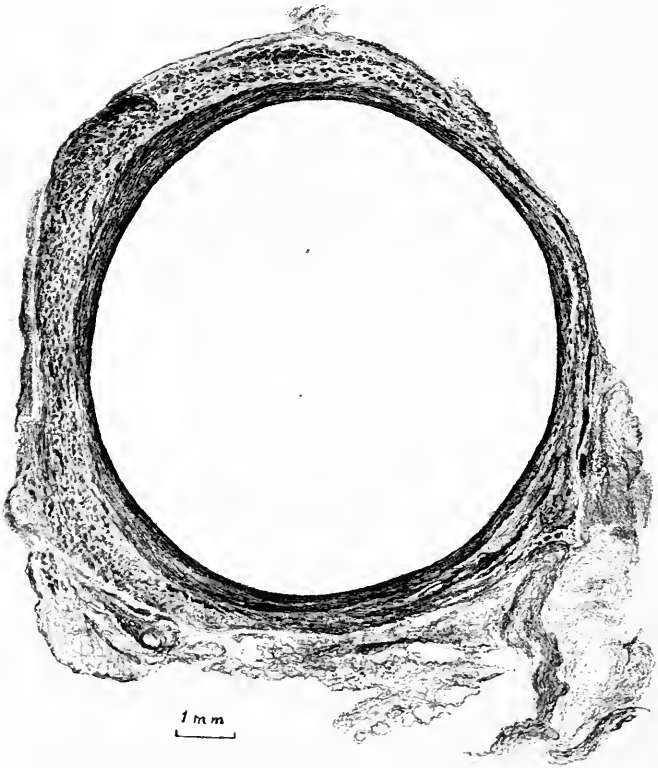
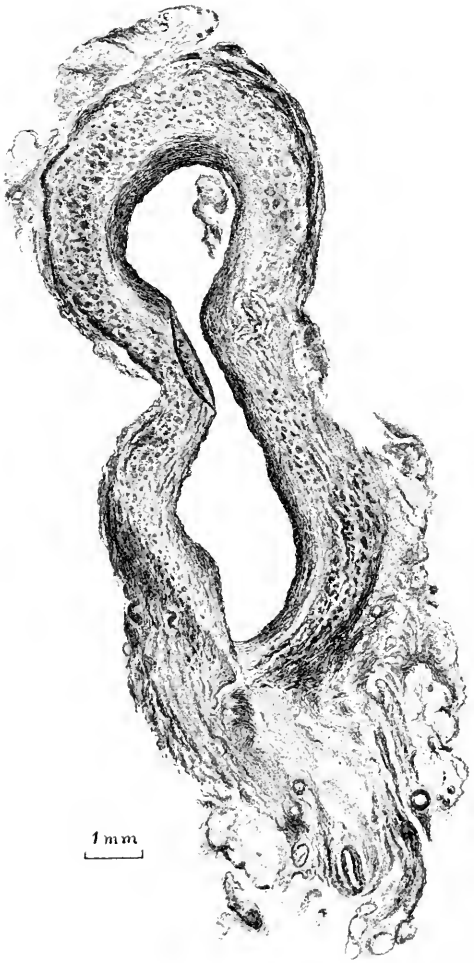


FIG. 6.—FEMORAL VEIN; SHRUNKEN. (× 8.)

From the same case as Fig. 1. The lumen of the vein is very small in comparison with Fig. 5 and is of irregular shape. The wall is thicker from shrinkage and is folded. It is even less like the ordinary histological standards, for the longitudinal bands of muscle are more strikingly shown.

FIG. 6.



(eight diameters), there is no such distinctly recognizable differentiation into intima, muscularis, and adventitia as in the case of the artery. The wall of the unshrunk section is very irregular in thickness, while in the shrunk section this difference is to a great extent lost, perhaps owing to the folding and irregularity of shape. When the sections from which these two drawings were made are examined under greater amplification, it is seen that the vasa vasorum are not confined to the outer fibrous layer, as it is usually set down in the text-books that the vasa vasorum are confined, but that they extend into the deeper layers of the vein adjacent to the lumen.

In Figs. 7 and 8 are seen illustrations of the popliteal artery and vein both shrunk and unshrunk. They were drawn from preparations of diseased blood-vessels, but, notwithstanding this, they show a number of anatomical points of interest. The difference in the size of the openings and in the thickness of the walls due to shrinkage is great, and is easily seen. It is notable that in the shrunk section the calibre of the vein is smaller than that of the artery and its wall thicker, while in the unshrunk section the vein has thinner walls and a very much larger calibre than the artery. The loose texture of the tissue of the vein has caused it to shrink much more in the preservative fluids than the denser artery. The irregularity of thickness of these vessels is striking, and there is no known law determining which portion of the vessel is thickest and which thinnest. At one time I thought that blood-vessels which lie in pairs are thickest at their contiguous parts, but these sections show that such is not the case, for, while the thickest part of the vein is that which abuts against the artery, the opposite obtains in the artery, the thickest part of its wall being that which is furthest away from the vein. When this popliteal vein is examined with greater amplification, it becomes evident that it possesses many characteristics commonly attributed to arteries: to so great an extent is this the case that were it not that the two vessels were removed together and that it is therefore impossible that a mistake could be made, the vein might readily be taken to be an artery.

As a result of disease blood-vessels frequently become so much altered in appearance that they lose their natural characteristics, and arteries and veins become indistinguishable. Figs. 9 and 10 show the coronary artery of the heart unshrunk and shrunk. Fig. 11 is a por-

tion of the vessel wall from Fig. 9 more highly magnified, and Fig. 12 is a portion from Fig. 10 more highly magnified. These four pictures demonstrate that several of the appearances that are commonly seen in sections of blood-vessels prepared for microscopical examination in the ordinary way are due to shrinkage and are therefore unnatural. In Fig. 12 the plicated membrane is folded, as it always is when the shrinking is allowed to go on unimpeded, but in Fig. 11, which was prepared with glass in the calibre of the vessel, the plicated membrane appears as a straight line. It is of course well known that the folds are due to post-mortem changes, but the method I have devised for preventing the shrinking after death makes an ocular demonstration of what was previously known only by deduction. Blood-vessels containing ante-mortem clots sometimes show the plicated membrane straight (see Fig. 102) in the same way as the sections prepared with glass rods in their calibres.

In studying the muscularis of sections of arteries prepared in the two ways, unshrunk and shrunk, another curious and interesting feature appears, which is shown by Figs. 11 and 12. When the muscular coat of an artery that has been prepared for section in the ordinary way, so that its calibre has been greatly reduced owing to the shrinking caused by the various reagents, is examined under a moderately high power of the microscope, the muscle appears as if it were composed of a material formed of meshes—it resembles basket-ware. If the shrinkage has been impeded, the muscular coat looks very different; there is little or no resemblance to basket-ware, for the muscle appears to be composed of concentric lines. In sections prepared with a glass rod in the artery (Fig. 11) the muscle nuclei are nearly straight and all run in the same direction, forming parallel lines; on the other hand, in sections in which the shrinkage was allowed to occur unimpeded (Fig. 12) the nuclei are irregularly placed, most of them lying with their long diameter more or less across the line of the general circuit of the artery. Besides this the nuclei, instead of being straight, are of very irregular shapes. Most of them are bent and some are twisted and turned almost into the shapes of irregular spirals. A comparison of Figs. 11 and 12—which are sections through the entire thickness of the wall of the same artery, one prepared with a glass rod in its calibre and the other allowed to shrink unimpeded—shows how much thicker the three coats are when shrunk and how

FIG. 7.—POPLITEAL ARTERY AND VEIN; UNSHRUNKEN. (× 8.)

From a youth of eighteen years whose leg was amputated above the knee for osteosarcoma of the thigh. The popliteal artery (*a*) and vein (*v*) and a small blood-vessel (*h*). Glass rods were inserted in the artery and vein to prevent shrinkage. All three of the vessels are a good deal thicker-walled than is natural, and the tissue composing *h* is diseased so that it is impossible to distinguish whether it is an artery or a vein. The calibres of *a* and *v* are circular because they were held in that form by the glass rods. The walls are strikingly and very irregularly thickened, and it is noticeable that the thinnest part of the artery wall is where it abuts against the vein, and its thickest part far from the vein. Fig. 8 is a section of the same blood-vessels, but prepared without glass rods and therefore shrunken.

FIG. 8.—POPLITEAL ARTERY AND VEIN; SHRUNKEN. (× 8.)

From the same patient as Fig. 7. The blood-vessels were preserved in alcohol but without glass rods in them and they shrunk. *a*, popliteal artery; *v*, popliteal vein; *h*, the blood-vessel *h* in Fig. 7. It cannot be ascertained whether *h* is an artery or a vein, but it is more like a vein, for its muscular tissue has the open-meshed structure that is common in diseased veins. The walls of the artery (*a*) and vein (*v*) are greatly but irregularly thickened, and are also folded and corrugated, owing to the shrinkage. It is notable that the vein here is thicker-walled and has a smaller calibre than the artery, although exactly the contrary is the case in the unshrunken section (Fig. 7).

Fig. 7.

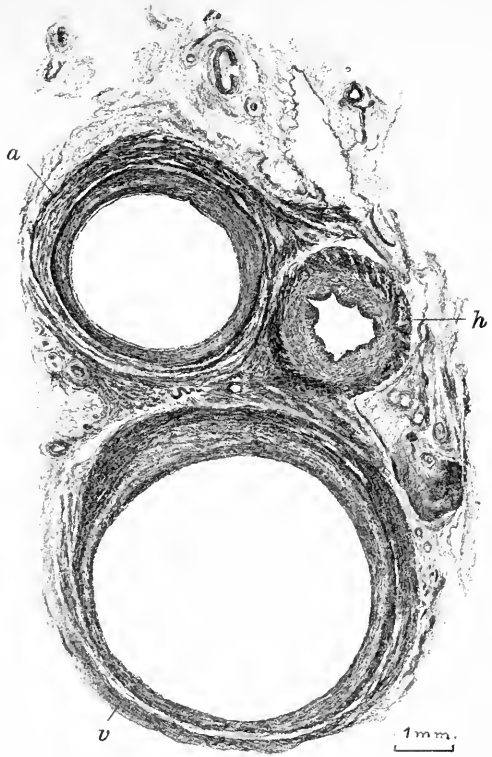


Fig. 8.

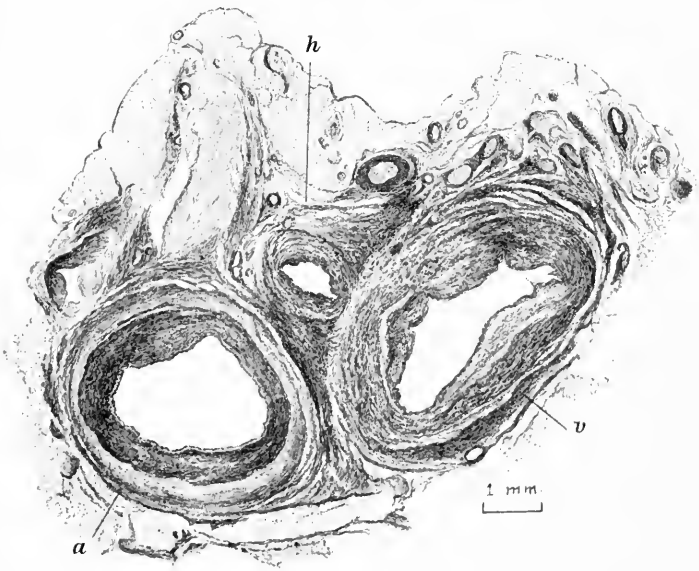


FIG. 9.—CORONARY ARTERY; UNSHRUNKEN. (× 8.)

From the same case as Fig. 1. Section in which a glass rod was inserted to prevent shrinkage. Fig. 10 shows a portion of the same artery in which no rod was placed. The difference in the size of the lumen and in the thickness of the wall of the vessel is striking. *k*, the region represented more highly magnified by Fig. 11.

FIG. 10.—CORONARY ARTERY; SHRUNKEN. (× 8.)

From the same case as Fig. 1. This portion of the vessel was preserved without any glass rod in it, and it therefore underwent the usual shrinking. Contrasted with Fig. 9 the smaller size of the lumen and the greater thickness of the wall are striking. *l*, the region represented more highly magnified by Fig. 12.

FIG. 9.

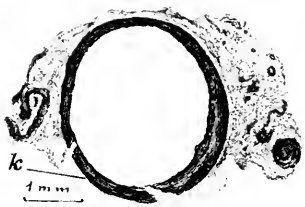


FIG. 10.

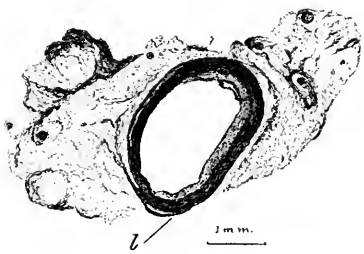


FIG. 11.—CORONARY ARTERY; UNSHRUNKEN. (× 240.)

The region *k* from Fig. 9 more highly magnified. It is a section through the entire wall of the artery, which is normal except for thickening of the intima. Such thickening is the commonest disease of arteries, and it is so common in young as well as in older persons that it may almost be said to be universal. *i*, intima; *p*, plicated membrane; *m*, muscularis; *a*, adventitia. The contrast is striking between this, which represents the portion of the vessel in which shrinkage was prevented by the introduction of a glass tube, and Fig. 12, which represents a portion of the vessel in which the usual shrinkage that takes place in specimens preserved in alcohol was allowed to occur. The total thickness of the vessel wall is much less here because the shrinkage was prevented and each one of the three coats is less thick. Besides this, the plicated membrane is straight, none of the usual folds being present. The muscle nuclei are nearly all straight, and are placed in positions concentric with the circle of the artery. Their condition here is strikingly different from that of the muscle seen in Fig. 12 and much more like that which exists during life.

FIG. 12.—CORONARY ARTERY; SHRUNKEN. (× 240.)

The region *l* from Fig. 10 more highly magnified. It is a section through the entire wall of the artery. *i*, intima; *p*, plicated membrane; *m*, muscularis; *a*, adventitia. The total thickness of the vessel wall is much greater than in Fig. 11, and each of the three coats is thicker. The plicated membrane is folded as usual and the intima shows the result of the shrinkage. The change in the muscle nuclei is striking. Owing to the shrinkage they are more crowded; they are twisted like corkscrews, and are set at varying angles across the circle formed by the artery, instead of being placed concentrically. It is this irregular situation of the elongated nuclei that usually causes the arterial muscularis to resemble basket-work when examined with the microscope.

FIG. 11.

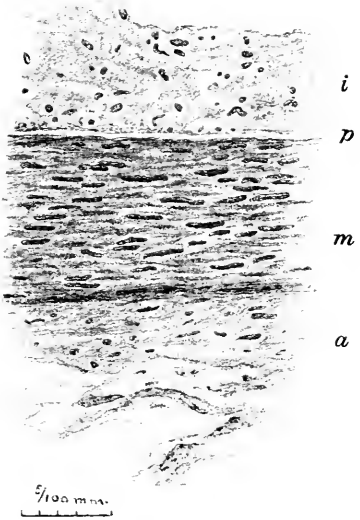
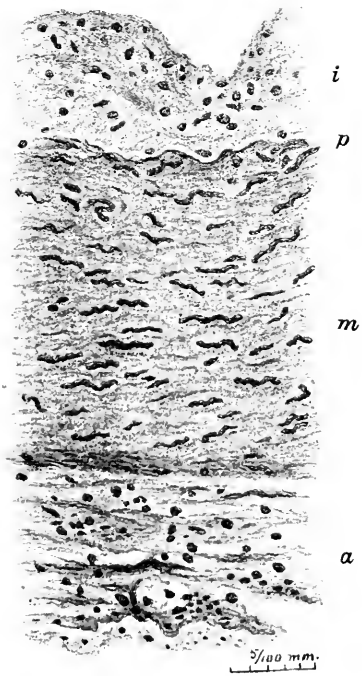


FIG. 12.



different the tissues appear. In the unshrunk section (Fig. 11) the plicated membrane is straight and the muscle nuclei lie in parallel lines, which entirely destroys the resemblance to basket-ware which is such a striking feature in sections of the muscularis of arteries prepared in the ordinary way and examined with less amplification than was used for this drawing. This illustration much more nearly represents the appearance of the different tissues of the blood-vessels during life than do the ordinary pictures and descriptions in text-books of histology.

Double sets of sections prepared in the way that has been described, one set with glass in the calibres of the blood-vessels to prevent shrinkage and the other allowed to shrink unimpeded in the reagents, demonstrate, as has been shown, various points of interest. They show the very great shrinkage which occurs in consequence of the action of the various liquid reagents in which one after another the tissues are soaked. The experiment proves that as a general thing veins shrink more than arteries. This is because the veins are formed of a material which is of looser texture than that of which the denser arteries are composed. The tissue of veins makes me think of the open-meshed appearance of elastic webbing, while arteries are hard and dense like India rubber bands. The sections demonstrate that the folding of the plicated membrane is the result of post-mortem shrinking and that the basket-ware appearance of the muscular tissue of arteries is principally due to the distortion of the nuclei and to their falling into unnatural positions irregularly across the general line of the arterial circumference.

Figs. 13, 14, and 15 represent a radial artery and vein which were prepared in the usual way by the paraffin method, no effort having been made to prevent shrinkage. It is impossible to obtain human blood-vessels which can be known with absolute certainty to be normal, but these seem to be fair types of the normal condition at twenty-five years of age. They show a number of points of interest. The muscularis of the artery in Fig. 13 presents the basket-ware appearance to which allusion has been made as being one of the common characteristics of such tissue. The intima is not a thin and even band lined with endothelium, as it is described in text-books, but a cellular tissue which is of varying thickness at different parts of the circumference. The nature of this tissue is better shown by Fig.

14, which is an illustration of a part of the wall of the artery more highly magnified.

One of the most striking characteristics of the middle-sized and smaller arteries of man is this irregularity of thickness of the intima. Embryological studies seem to prove conclusively that the arteries of man as well as those of lower animals are formed according to well-ordered laws and have during the earlier periods of life the appearances that are to be found described in text-books. The examination of a great number of arteries under circumstances and conditions as varied as possible has convinced me that typically normal human arteries are almost impossible to find. Pathologists have observed that thickening of the lining of the arteries is a very common result of disease and they have named it endarteritis. My own studies have forced me to conclude that it is impossible to make an absolute distinction between the slighter degrees of endarteritis and the little irregularities of thickness of the intima which should not be considered as disease and which are found in all human arteries, even in those of children and of infants. The point I wish to emphasize is that all arteries removed from human bodies after death will be found to have more or less irregularity of thickness of the intima such as is shown by Fig 13.

Fig. 15 is a more highly magnified portion of the wall of the radial vein shown in Fig 13. Although the three layers—intima, muscularis, adventitia—can without difficulty be distinguished, the vein is but little like the illustrations and descriptions found in text-books.

A consideration of the information to be obtained from text-books of anatomy and histology has forced upon me the opinion that, while the peculiarities of arteries have been only imperfectly described, the study of veins has as yet hardly begun. Fig. 16 shows a section through the wall of the vena cava, Fig. 2, more highly magnified, and Fig. 17 depicts a section of the sinus venosus of the heart. These two veins are very unlike the ordinary descriptions of veins. The wall of the vena cava is divided into three layers, but the intima is composed of loose-meshed tissue which is unlike the descriptions of the intima of veins. The middle layer is indeed formed of muscular tissue, but it is odd looking and not like common involuntary muscle, and is besides disposed in bundles which run in the direction of the length of the blood-vessel, there being no circular muscular layer

FIG. 13.—NORMAL RADIAL ARTERY AND VEIN. (× 20.)

From a negro woman twenty-five years old who died of meningitis. The artery is to the left, and it is as nearly normal as any of the arteries of persons who have died of disease. The intima is always as thick as it is here represented. *f* is a region represented more highly magnified by Fig. 14. The vein is the thin-walled vessel to the right. The variation of the thickness of the wall is probably due to obliquity of section. *g* is a part which is shown more highly magnified by Fig. 15. The vein appears to be normal.

FIG. 13.

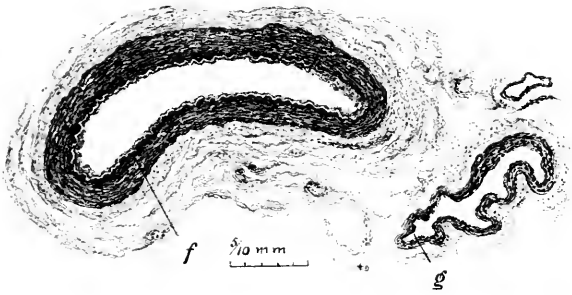


FIG. 15.—NORMAL RADIAL VEIN. (× 240.)

The region *g* from Fig. 13 more highly magnified. *i*, intima; *m*, muscularis; *a*, adventitia. It is very unlike the ordinary descriptions of veins in the text-books.

FIG. 15.

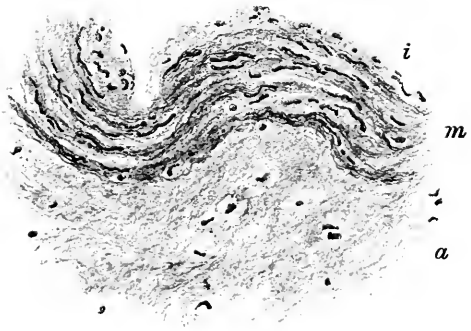


FIG. 15.—NORMAL RADIAL VEIN. (× 240.)

The region *g* from Fig. 13 more highly magnified. *i* intima.

FIG. 16.—VENA CAVA. (× 50.)

From the same case as Fig. 1. The region *t* from Fig. 2. It is not like any ordinary vein, but strongly resembles Fig. 17. *x*, the lining; *y*, the middle portion; *z*, the external portion of the vena cava. The lining is not like the ordinary intima of veins. The tissue of the middle portion (*y*) is involuntary muscle; it is not arranged in the usual manner, but is disposed in large, separated bundles, most of which run in the direction of the length of the vessel.

FIG. 17.—SINUS VENOSUS OF THE HEART. (× 8.)

From the same case as Fig. 1. The vessel presents none of the ordinarily described characteristics of veins. It is simply a channel through the muscular substance of the heart; the vessel has no differentiated wall except the thin fibrous layer. It is something like the vena cava represented by Figs. 2 and 16.

FIG. 18.—NORMAL BLOOD-VESSELS OF THE SPINAL CORD. (× 50.)

From a man forty years old who died of tetanus. The smaller thick-walled vessel above is an artery and it is normal. The thin-walled vessel below is a vein. The striking feature is that so large a vein should be simply a ring of fibrous tissue without any muscular layer, and entirely without any division of its walls into three coats.

FIG. 16.

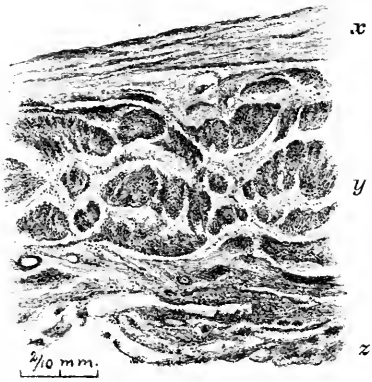


FIG. 17.

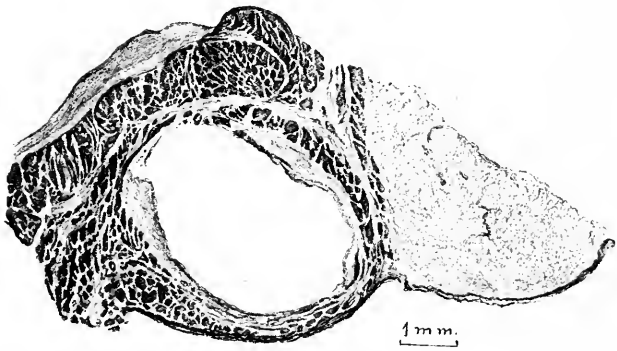
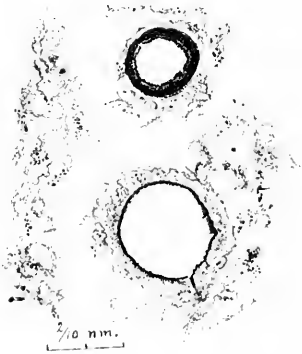


FIG. 18.



visible. The sinus venosus of the heart is not like any other blood-vessel that I have seen. Its wall is formed of a fine thready tissue without any trace of differentiation into coats, and there is no involuntary muscle to be distinguished. This fine thready tissue forms the only wall of the vein and it alone separated the blood from the muscular tissue of the heart surrounding the blood-vessel. The vena cava and sinus venosus of the heart are in all respects different from the commonly accepted conception of veins.

Fig. 18 represents an artery and its accompanying vein of the human spinal cord. The artery presents no notable features, but the vein shows in a striking manner a peculiarity that will be further emphasized in subsequent chapters. This peculiarity is that arterioles of good size and formed of three coats are often accompanied by single-coated return vessels which are much more like very large capillaries than like the common veins. Such vessels I have found in the heart and in the brain and spinal cord. The vein in Fig. 18 is formed entirely of fibrous tissue, and it is easy to see that it does not contain any muscular tissue in its wall and that there is no sign of a division into three coats. This fact—that the return vessels accompanying good-sized arterioles often do not have three coats—is mentioned in the text-books, but it has not been sufficiently emphasized to make it common knowledge.

CHAPTER II

Capillaries

Capillaries are the ordinary channels of communication between the arteries and the veins, but under exceptional circumstances the arterial and venous radicles are said to communicate with one another directly, as, for instance, in the erectile tissue of the genital organs, in the spleen, in the tips of the fingers and toes, and in the nose. The most important function of the capillaries is the distribution of the nutritive material of the blood to the tissues. This function is one in which the arteries and veins have no share, for they serve merely as channels of communication, carrying the blood from one part to another. The capillaries form rich net-works in almost all of the tissues and organs. Their average diameter is 7–10 microns and the capillary supply of young tissues is richer than that of old ones. The capillaries generally consist of a single layer of endothelial cells, but some capillaries are said to be surrounded by an imperfect adventitious coat formed by a net-work of branched connective-tissue cells. The peculiarities distinguishing the capillaries from the small capillary arteries and veins consist less in the size of the vessels—for the capillaries may be the larger—than in the character of their walls. The true capillary possesses no muscle-cells. Such is the ordinarily accepted description of the objective features of the capillaries. In thinking of them the fact must never be lost sight of that they are the only part of the blood-vessels that is directly occupied in fulfilling the primary function of the circulatory apparatus, namely, the nutrition of the tissues. The arteries and veins are only tubes to carry the fluid from place to place in the economy. The anatomy and pathology of the arteries and veins are easy studies in comparison with that of the capillaries, for arteries and veins are permanent and are large enough to be easily seen, while of the capillaries it may without exaggeration be said that they are ephemeral and elusive. There is a certain likeness between the human vascular system, composed of the heart, the arteries, the veins, and the capillaries, and the rain when it falls upon the earth and runs off to the sea in rills, rivulets, and rivers. If any profit is to be derived from the comparison, however, allow-

ance must be made for the great difference of the forces at work and the widely different conditions. Gravity is the force which carries the rain-water to the sea, whereas it is the pumping action of the heart which drives the blood through the arteries into the capillaries. When the rain falls upon the earth the flow is from the smaller into the larger channels, but the blood is driven from the large arteries into the minute capillaries. Conceding the difference, I think the resemblance is striking. When it rains the drops collect together until a body of water is formed which is too large to lie upon the surface where it has fallen, the water then flows out in the direction in which the ground falls, forming a little rill. The rill flows on until it meets with others like itself, with which it joins and they go on until a permanent stream is reached, and every one knows how streams run together, growing larger and larger until a river is formed. The rivers and the larger streams are permanent and they are perhaps the most striking of nature's features ; but the little rills disappear after every rain and the smaller ones—in the grass, for instance—leave no trace behind to show where they were. Arteries and veins and arterioles and venules are as permanent as the rivers and streams. Even if disease forms an obstruction and blocks up one of these larger blood-vessels, the empty one continues to have as distinctive a form of its own and is as easy to recognize as a stream bed from which the water has been turned aside. The capillaries are like the rills, for they come and go. They may truly be said to be ephemeral, for they open in the tissues as the need for them arises and close and disappear when their usefulness has ceased. The importance of this obvious truth has not been fully recognized, for, although pathologists have studied the growth of capillaries under the influence of disease in tissues like the cornea, the converse of the proposition, that they are evanescent, has not been dwelt upon to make the fact seem as important as it really is.

The ordinary description of a capillary is that it is a minute tube composed of a single layer of endothelium. Endothelium is like a pavement of tiles, being formed of a single layer of flat cells which are accurately joined together at their edges. Capillaries are so small that they can be seen only with the microscope. Most of the human tissues contain capillaries, but there are none in the nails, the outer horny layer of the skin, the enamel of the teeth, and the

healthy cornea of the eye. Although capillaries are present in most of the tissues, it is not always possible to distinguish them in uninjected specimens after death. In sections which have been prepared by the ordinary methods the capillaries are generally visible in the heart and very often they are easily seen in sections of the lung. In the liver and spleen they are generally less readily made out, and in the kidney sometimes they are very obvious and again it is hard to see any of them.

In properly prepared sections of suitable specimens of human heart large groups of capillaries branching in the most complex way may be seen with the greatest distinctness. They are seen in longitudinal and in cross-section, so that the demonstration that they are tubes is perfectly complete and satisfactory, and, as blood-corpuscles are often seen lying in many of the capillaries, the anatomical picture is complete. When it is remembered, however, that the walls of these tubes are exceedingly delicate and besides that all connective tissue contains exactly similar cells, it raises the doubt whether the capillaries are any more permanent than the rills of water that run through the grass during a rain. How can a capillary be recognized with certainty in any ordinary section of tissue? Only by its size, circular opening, and wall composed of a single layer of endothelium with the characteristic nuclei. If in addition to this a few blood-corpuscles in such a state of preservation as to make it certain they are blood-corpuscles are lying within the calibre, the demonstration is complete. Such are typical capillaries and they are easy to see in sections of human heart and often in other tissues. When seen in this form there can be no doubt as to what they are, and that they are as definite entities as the largest artery or vein. If a moment is given to the consideration of the surroundings of the ordinary capillaries in the heart, it will be manifest that capillaries must often be very elusive objects to search for with the microscope. Most of the capillaries lie in the interstices between the bundles of muscular fibres, and these interstices are filled with connective tissue. Even when the capillaries penetrate into the narrowest spaces between single muscular fibres and into the very centres of the fibres themselves,[1] a little connective tissue appears always to accompany them.

[1] Origin of Disease, by Arthur V. Meigs, Chapter V. : J. B. Lippincott Co., 1899.

If a bundle of capillaries in the heart could be emptied of blood and then exposed to sufficient pressure to force the capillary walls together, the tissue would look exactly like any of the ordinary connective tissue which lies in the intermuscular spaces of the heart. Almost exactly the same is the case with the capillaries of the other organs and tissues. Wherever capillaries go they lie in the connective-tissue spaces, and even when a capillary is seen by itself it is found to be accompanied by some connective tissue. It is hardly conceivable that under the constantly varying conditions of the circulation and the changes to which the tissues are subject the bundles of capillaries do not often become empty, and if they do become empty they must collapse, as other tubes in the human body do when there is nothing within them to hold them open. When a bundle of capillaries is emptied and the walls fall together, their calibres must very soon be obliterated. From what is known of the tendency of the tissues to adhere when they are wounded, it is only reasonable to think that obliteration must soon occur; besides which the axiom that nature abhors a vacuum would be almost enough to make it certain that a series of collapsed tubes would not long remain patulous. It is certain that capillaries are ephemeral and often return to their primitive state by giving back their walls again to form simple connective tissue; it is also certain that they can push their way on, and form and increase in tissues in which they had not been, for this process has often been watched under the microscope in living animals. It is my opinion that capillaries never have the same definite existence that arteries and veins have. The arteries and veins are sharply differentiated, having a special structure of their own, and they must always be built up in any tissue in which they lie. The capillaries, on the other hand, are nothing but tubes hollowed out in the connective tissue with which they are surrounded. If a single capillary running in any tissue by itself is empty, it becomes at once and without any change a string or fibre of connective tissue.

This belief that capillaries are evanescent and never have the same permanent and definite existence as arteries and veins is supported by the study of injected specimens of various tissues. In properly selected specimens of tissue of which the blood-vessels are injected, it is easy to see the capillaries. If one color is used to dye the injected material and another for staining the tissue, the contrast of the

two colors causes the blood-vessels to be striking objects in any field which is examined under the microscope. Injected specimens, however, do not give the perfect satisfaction that it might be hoped they would, and this is principally for two reasons: first, that the colored injection material necessarily partly covers and therefore obscures portions of the tissue which in uninjected specimens of the same tissue are easily seen; and, second, because it is often impossible to know whether a particular portion of the injected material that is being examined is really within a blood-vessel or if the vessel has burst and this material is lying loose in the tissue. The manner in which an injected liquid distributes itself in some tissues clearly shows how capillary channels may open in the same tissue during life when there is need for them. In examining sections of injected tissues, it is always easy, if one is disposed to be careless, to say of any appearance that is difficult to interpret that it resulted from the bursting of the blood-vessels owing to too great force having been used in making the injection, and that the injected liquid had escaped into the interstices of the tissue. There is no doubt that in making injections this accident often occurs. Under these circumstances the liquid of course flows in the direction of least resistance and it fills the portions of tissue which are most open-meshed and loosely constructed. The lesson which should be learned from this is, I think, that very much the same thing may happen, and probably often does happen, during life in conditions of disease that can be produced after death by the use of a syringe to force fluid into the blood-vessels.

Sections of human spleen sometimes present appearances which lend support to the belief that capillaries are ephemeral, and are simply openings in the tissue, permitting the passage of blood, instead of being differentiated vascular channels with distinct walls, as the arteries and veins are known to be. As has already been said, it is difficult to draw an absolutely just comparison between the conditions which exist during life and post-mortem appearances and effects that result from the manipulation of dead tissues. When the size of a channel or space which has been filled with injecting fluid is being considered, and it is desirable to know whether this channel or space was of the same size during life, the knowledge cannot be obtained. It has been already shown that shrinking always occurs at the time of death when the blood-vessels empty themselves, and that there is further shrinkage

afterwards in the course of manipulation in preparing the tissue for microscopical examination. It is impossible to form an estimate which can be known to be anything like accurate in regard to the extent of this shrinkage, and therefore it is impossible to know what was the size during life of any blood space that is examined after death.

In sections of human spleen injected with a blue dye and stained red with carmine, areas are often seen in which the leucocytes which are stained red are surrounded by fine threads of the blue injecting material. The result is that the leucocytes are spherical or polyhedral and are not directly in contact, but are separated by a fine mesh-work of spaces or channels which are filled by the blue injecting material. The red leucocytes are often completely surrounded by the rings of blue. In order to see this it is necessary to use quite high amplification, and it is impossible to be certain whether the spaces that the injecting material has filled have walls, and therefore answer the classical description of capillaries, or if the injection was forced between the cells and lies there without anything to separate it from the cells themselves. In any blood-vessel which has been injected, even in large ones like arteries and veins, the walls cannot be so well studied as in uninjected specimens, because the injection material always partially covers up the tissue of the walls and obscures the view of them. In the case of injected capillaries the walls often cannot be seen at all and they are always much obscured. The intercellular spaces in injected spleen, that have been described as being filled by the injecting material, are often much narrower than an ordinary capillary and are so small that it would have been quite impossible for a blood-corpuscle to have passed through them. The appearance of the splenic leucocytes stained of one color and surrounded by the fine and often very complete mesh-work of the injection material of a different color is very striking, and it makes it seem highly probable that fluids pass around the leucocytes during life, but it is impossible to know whether there are simply intercellular spaces or if there is a net-work of capillary tubes with walls of their own.

It is easy for any one to suggest, as an explanation of the appearance that has been described, that the injection had burst the capillaries and that the injecting material had escaped into the interstices of the tissue, but it is impossible to prove that such was the case. There is no reason why the heart may not drive fluid almost any-

where that it can be forced with a syringe. It seems to me reasonable to think that the interstices between the splenic leucocytes are connected with the blood stream during life, and, if the spaces are too small to permit the passage of the blood-corpuscles through them, that the liquor sanguinis in this way bathes the splenic cells. Although the splenic intercellular interstices as they are seen post mortem in injected tissue are of much less diameter than a blood-corpuscle, it is impossible to be sure that this is not owing simply to post-mortem shrinkage, and that during life the cells of the spleen are at all times sufficiently widely separated to permit of the passage between them of the blood-corpuscles. I have many sections of injected human spleen which demonstrate the characteristics described, and I have often thought of having a picture made showing the conditions, but I have been deterred because of the difficulties. Such a picture would have to be in two colors, and, as the red leucocytes and the surrounding threads of blue can be seen only when greatly magnified and with changes of the focus of the microscope, it would be very difficult to get an artist to appreciate the conditions and then to depict them. The following quotation from Leidy's Anatomy shows that the belief in the existence of capillary spaces too minute to admit of the passage of a blood-corpuscle is not incompatible with opinions formerly accepted as correct. "The smallest admit the passage of blood-corpuscles, although but a short time has elapsed since the opinion universally prevailed that in all structures of the body capillaries existed which only transmitted the liquor sanguinis." [1]

In the following chapters various curious conditions of capillaries caused by disease are described. In pathology the question how far Gull and Sutton, in their classical essays on arteriocapillary fibrosis, were correct in supposing that the disease they described is really one of vascular origin is of perennial interest and is not even yet decided. If the capillaries are as ephemeral as I believe, and their walls are only cylindrical channels which come and go from day to day in the connective tissues, it becomes a question whether the diseases that affect them originate in the blood or in the connective tissue. The study of disease of the capillaries is therefore a very difficult one, and but little has yet been learned regarding it.

[1] An Elementary Treatise on Human Anatomy, by Joseph Leidy : J. B. Lippincott & Co., 1861, page 337.

CHAPTER III

New Blood-Vessels

It has long been known that new blood-vessels develop in the tissues under the stimulus of disease, and that this new growth takes place even in aged people in the same manner that it does in the young. Ziegler[1] says, "The formation of new blood-vessels plays a chief part in hyperplasias of every kind. Wherever fibrous tissue, bone-tissue, gland-tissue, or any other is produced in quantity, new blood-vessels must of necessity be developed. In no other way is it possible to keep the new-formed tissue adequately supplied with nutriment. For this reason new blood-vessels begin to be formed at a very early stage in all new growths, and they must be regarded as the chief factors in the formative process.

"New blood-vessels are developed out of offshoots which start from the walls of existing blood-vessels. . . . We have not given the customary enumeration of the primary, secondary, and tertiary modes formulated by Billroth and Rindfleisch. In the primary mode the embryonic cells become directly transformed into red blood-cells on one hand, and into the parietal cells of a vessel on the other. The embryonic cells in fact arrange themselves into cords: the axial ones become blood-cells, the peripheral ones cohere as elements of the containing vessel-wall. This process takes place in the mesoblast of the embryo, but not in pathological formations." Ziegler's description of the secondary mode is not quite clear, but he describes it as not very different from the primary one. He then goes on to describe the tertiary mode, giving a concise account of what is so well known of the development of blood-vessels under the stimulus of irritation in the cornea of the eye, in the web of the frog's foot, in the tadpole's tail, etc. An important point to note is his statement that "new blood-vessels are developed out of offshoots which start from the walls of existing blood-vessels," and that after discussing the independent growth of blood-vessels, which is so well known and has been so

[1] Text-Book of Pathological Anatomy, by Ernst Ziegler, translated by Donald MacAlister. Part 1, General Pathological Anatomy, pages 125–127. London, Macmillan, 1883.

minutely observed in the tissues of embryos, he says, "this process takes place in the mesoblast of the embryo, but not in pathological formations." These conclusions of Ziegler constitute a fair exposition of the opinions that prevail in regard to the development of new blood-vessels as a result of disease. There cannot be the slightest doubt that his views are correct as far as concerns the mode of growth by offshoots, which has been studied with such scientific exactitude that the results which have been obtained are conclusive. It has seemed to me, however, that Billroth and Rindfleisch were right in their belief that when the conditions necessary to its production exist the same kind of development of blood-vessels that is known to take place in embryos occurs also in pathological formations. It is not possible to prove the correctness of this opinion in the same way that it has been proved that blood-vessels grow from offshoots, for that mode of development can be made to take place at will in the tissues of animals and all the various stages of the process can be closely watched. On the other hand, the only evidence that can be obtained to prove that blood-vessels grow independently of the pre-existing ones in pathological formations, in the same way that they grow in embryos, must be acquired from the examination of diseased tissues after death. As progress ceases with death, there is no opportunity to see the course of growth.

It is not unnatural for those who have studied the growth of new vessels in the tissues of the lower animals, a process they can set in motion at will and thereby at any time obtain abundant material for study, to be slow to believe that blood-vessels grow independently in diseased tissues in the same way that they grow in embryos. It is impossible, as has been said, to prove that they do, but I have some specimens of tissue which present appearances which I think make it reasonable to believe that blood-vessels do grow independently. The tissue in which I have been able to study this development of blood-vessels to the greatest advantage is the thickened intima of arteries which have been affected by endarteritis. It often happens that the three tunics can still be easily distinguished even in arteries which are exceedingly thick, in properly prepared sections. The coat which is ordinarily the most diseased and thickened is the intima, and it is often composed of a material which is unlike any of the natural tissues. In some respects this tissue resembles connective tissue and

in others it is not unlike ill-developed epithelium. It is in tissue of this nature especially that I have seen the most curious and varied forms of new blood-vessels. It may be well to recall the fact that in the natural condition the vasa vasorum are confined to the external coat of the arteries and veins they nourish, and that none of them penetrate into the muscular tunic, nor are any to be found in the intima.

In a set of serial sections of an arteriole from the lung of a child twelve years old, who died of heart disease, I have found the most convincing evidence of the independent growth of blood-vessels. The artery is greatly thickened, but the plicated membrane can be distinctly seen around the entire arterial circle. As usual this membrane is a valuable landmark, making it possible clearly to distinguish one coat from another. In this arteriole the intima is much thicker than either of the other coats, and it is composed of the peculiar tissue which has already been mentioned as difficult to classify, for it has some of the characteristics of connective tissue and some of those of epithelium, and yet presents marked differences from them both. This curious growth is more like the tissue which is seen in early embryos than like anything else. All embryologists know that during the early stages of development the cells in the tissues of embryos are unlike any cells of the tissues or organs of adults and are without the distinctive characteristics that they acquire later. For instance, the difference of the heart from the liver is to be distinguished by the form and position of the two organs and not by the differences between the muscle cells of the heart and the epithelial cells of the liver which in adult life are so great. In this arteriole of which the intima is so thick and is formed of tissue like that of embryos, there are spaces which are like the blood-islands which develop in the vascular area outside the body of the embryo of the chick and which are at first independent and disconnected from the heart. By examining these spaces through several of the serial sections it is easy to determine that they answer the descriptions of the blood-islands of embryos and they contain cells which closely resemble blood-corpuscles. As the tissue is pathological, and as it is never possible to obtain the tissues of those who die of disease in a fresh condition as is always done by embryologists in pursuing their researches, it would probably be unreasonable to expect to get the nearly perfect results that em-

bryologists obtain. If it is impossible to be certain that the cells contained by these blood-islands are blood-corpuscles, it is easy, on the other hand, to determine that the spaces are closed sacs and quite disconnected from the blood-vessels. A study of the serial sections demonstrates that the spaces are not connected with any blood-vessels nor with anything else, but are independent. The spaces are too large to be swollen cells, and it seems impossible to explain their existence in any other way than to say that they are developing blood-vessels, with all the characteristics of the earliest developed blood-vessels of embryos which grow in the vascular area and elsewhere independently of the heart and aorta and are afterwards joined to them. It is certain the spaces I have described are disconnected from the general vascular system, and if it could be proved that they are blood-vessels it would establish the fact that I am correct in my contention that new blood-vessels develop in diseased adult tissues in the same way that they develop in embryos, and not, as has been generally believed of late, by the process of offshoots alone. I have already described these sections,[1] and have published illustrations exhibiting their peculiarities, and I had at one time the intention to have another series of drawings made to demonstrate still more completely the presence of the blood-islands in the morbidly thickened intima, but I found that it would be difficult or impossible. In studying sections, and especially serial sections, with the microscope, one often arrives at an opinion which is the result of the examination of many sections and the consideration of the relations of the appearances of one section with those of others. Such opinions cannot always be supported by pictures of the tissues that have been studied.

New blood-vessels develop in tumors and in every new tissue which is produced as a result of disease. Such tissue is beyond doubt a new production and cannot justly be regarded as the result of extension or outgrowth. New vessels grow in the walls of aneurisms, which might be considered to be mere extensions of natural tissue, but the increased amount of tissue that is formed in large saccular aneurisms makes it seem more reasonable to regard as a real new growth the material constituting their walls. In all of these tissues new blood-vessels may be found which present a great variety of

[1] Origin of Disease, by Arthur V. Meigs, 2d edition, page 52 et seq., and Figs. 23 to 27 : J. B. Lippincott Co., Philadelphia, 1890.

appearances, and it has long seemed to me that the most reasonable hypothesis in regard to their mode of growth is that many of them originated independently of the vessels already existing in the surrounding tissues and that they were later joined to the general system of blood-vessels in exactly the same manner as happens in embryos. In my book on "The Origin of Disease" there are descriptions and illustrations of blood-vessels in the new growth of pericardial adhesions [1] and in the wall of an aneurism.[2]

There are many other curious and interesting facts connected with the development of new blood-vessels. In the earlier stages of their existence and while they are still small, they more nearly resemble capillaries than arteries or veins. Their walls are composed of fine fibrous material containing endothelial nuclei, and there is no muscular layer nor any adventitia. The new vessels frequently acquire a considerable size and still retain this capillary formation, but the thickness of the walls varies much with the difference in size of the vessel. Although new blood-vessels often have single-coated walls of fibrous tissue, even after they attain considerable size, they are capable of the further development of producing three coats in all respects like normal arteries.

Fig. 19 represents an arteriole in the peduncle which attached a small fatty tumor to the liver. The tumor lay upon the upper surface of the liver, between that organ and the diaphragm. The vessel has three coats like any normal arteriole, and the muscular cells of both the longitudinal and circular layers are distinctly shown. It is as certain as anything in pathology can be that this arteriole is a new growth, for a fatty tumor loosely attached to the upper surface of the liver, with such an arteriole passing through the peritoneal covering upon the free surface of the liver and going to nourish the tumor, could only be the result of diseased new growth. The discovery even of one three-coated arteriole of normal appearance is sufficient to show that the capacity to develop natural blood-vessels under the stimulus of disease remains until past middle life. The man from whom this arteriole was taken was fifty-two years old, and it is most likely that the capacity to develop new blood-vessels, even fully

[1] Origin of Disease, page 51 and Figs. 18, 19, and 20.
[2] Origin of Disease, Fig. 15.

formed arteries and veins, is retained by human beings even to extreme old age.

Fig. 20 is a blood-vessel from the spinal cord of a boy of fifteen years who died of simple meningitis. The appearances and the pathological changes of the blood-vessels in simple and in tubercular meningitis and in syphilis will be discussed in another chapter (page 69). The vessel represented is so much altered by disease that it is impossible to ascertain whether it is an artery or a vein, but it is very much more probably an artery, for arteries frequently become thick walled as a result of disease, and veins are comparatively seldom affected in the same way. The tissue composing this blood-vessel (Fig. 20) is not like that which forms healthy vessels, and nothing can be seen of the normal division of the wall into three coats. There is no involuntary muscular tissue, nor anything like the natural intima or like the tissue which commonly forms the thickened intima of diseased arteries. I do not know of anything in healthy human beings like this tissue, but it in some respects resembles that of embryos. The most striking feature, however, and the feature that the drawing was made to show, is that there are numerous new blood-vessels in the thickened wall of the diseased vessel. These new blood-vessels, as is usually the case with small new blood-vessels, are like capillaries, and quite a number of them contain blood-corpuscles. The appearance of these small new capillaries containing blood-corpuscles, and the nature of the tissue which forms the wall of the whole blood-vessel, strongly resembles, I think, the blood-islands that are found in embryos, and that are so easy to see in the area vasculosa outside of the body of the developing chick embryo. This supports the opinion I have already expressed, that new blood-vessels grow in human tissues in disease separately from the vascular system and are afterwards joined to it, as occurs in embryos, and do not grow solely as offshoots from pre-existing blood-vessels, as is generally believed.

It is very common for new blood-vessels to grow in and about the capsules of the thoracic and abdominal viscera, and such vessels are shown by Figs. 21, 22, 23, and 24. Fig. 21 depicts a portion of the free edge of the lung of a negro man forty-nine years old, who died of Bright's disease. The tissue of the lung is thickened and unnatural in appearance, owing to the action of slow inflammatory fibrocellular infiltration. The pleura is incorporated with the diseased lung-tissue

FIG. 19.—NEW ARTERIOLE. (× 240.)

From a man of fifty-two years who died of chronic ulceration of the rectum. The vessel is in the pedúncle of a small fatty tumor which lay upon the upper and outer surface of the liver, to which it was fastened by the peduncle. The peculiarity of this vessel is that it is exactly like small normal arterioles, instead of having walls composed of endothelium or fibrous tissue alone, as most new vessels seen in diseased tissues have. The cells of the involuntary muscle are distinctly shown, some of them in cross and some in longitudinal section.

FIG. 20.—THICKENED BLOOD-VESSEL OF THE SPINAL CORD, WITH NUMEROUS CAPILLARIES IN ITS WALL. (× 240.)

From a boy fifteen years old who died of acute meningitis. It is impossible to ascertain whether the vessel is an artery or a vein, it is so much changed by disease. The wall is very thick, and there are many capillaries in it which contain blood-corpuscles. A few blood-corpuscles are lying in the lumen of the vessel adhering to its lining.

FIG. 19.

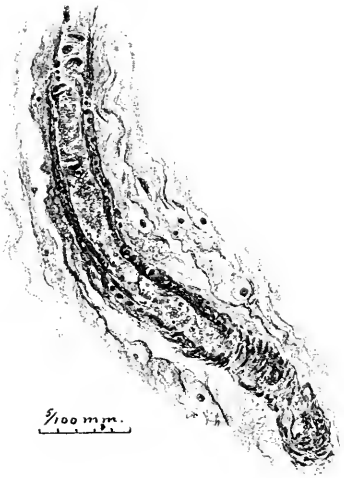
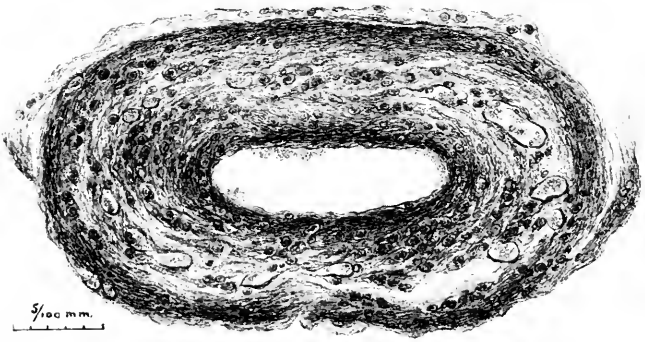


FIG. 20.



so that there is no demarcation between lung and pleura. The thickening of the lung is greatest at the free surface, and this is usually the case in disease of such nature. The thickened free edge of the lung contains many new blood-vessels distended with blood-corpuscles, as may easily be seen if the section is examined under sufficient amplification. Most of these blood-vessels are like capillaries. There is, however, one blood-vessel near the free edge of the lung (Fig. 21) which is of quite different appearance. It is thick walled and has a very small opening, which is placed to one side, instead of in the centre as the calibres of normal vessels always are. The calibre is lined with a single-coated layer of endothelium which contains endothelial cells and this layer looks like a string of beads. The ring of endothelium with its cells is exactly like the primitive aorta of the chick embryo, pictures of which are included in almost all the text-books of embryology. Greater amplification than was used in making the drawing (Fig. 21) is necessary to reveal all the details of structure of the minute blood-vessel, but the general characteristics are pretty well shown. The tissue somewhat resembles that shown by Fig. 20, and is quite unlike any ordinary normal human tissue, but is in many respects like that of embryos. There can be no question that this curious irregularly rounded collection of atypical cells with its opening out of centre is a blood-vessel, but, on the other hand, it is impossible to be certain whether it is one of the normal vessels which was changed by disease or if it is a new blood-vessel which has developed in the lung tissue owing to the hyperplasia. I believe it to be a new growth and that such abortive blood-vessels are common in various hyperplasias. The opinion of Ziegler, which it has been said is representative of the views of pathologists, has been quoted that "the formation of new blood-vessels plays a chief part in hyperplasias of every kind. Wherever fibrous tissue, bone-tissue, gland-tissue, or any other is produced in quantity, new blood-vessels must of necessity be developed."

One of the most extraordinary things in connection with this growth of new vessels in disease is the manner in which nature seems frequently to fail to attain the object she set out to accomplish. Owing apparently to irregular and exuberant growth of the cells, useless solid cords are produced[1] instead of tubes capable of performing their

[1] Origin of Disease, by Arthur V. Meigs, 2d edition, page 50 and Fig. 15 : J. B. Lippincott Co., Philadelphia, 1890.

natural function of carrying blood, or other irregular and apparently useless formations grow, which can be explained only as abortive attempts to form blood-vessels, without which no tissue can attain any considerable size and continue to exist. The drawing Fig. 15, in "The Origin of Disease," is a perfect type of this kind of abortive formation. 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 afterwards channelled out; but this does not occur, as far as is known, in the case of blood-vessels. The appearance of many of these abortive new blood-vessels is such as to forbid the belief that they had at any time large calibres and thin walls, as is natural. It is much more probable they were deformed from their very origin, and were the result of the innate tendency the organism has to produce blood-vessels in any formation as soon as it attains sufficient size to make them necessary to its continued existence.

Fig. 22 shows a section from the free edge of the lung of a negro man twenty-four years old who died of phthisis pulmonalis. It includes the pleura, which is greatly thickened and contains a good many new blood-vessels and a portion of lung tissue. The normal pleura is very thin, is almost avascular, is composed of many threads of fibrous tissue, contains but few nuclei, and there are generally but few cells distinguishable in it. This thickened pleura is a fibrocellular tissue rich in cells. The new blood-vessels are filled with red corpuscles and their walls are formed of endothelium, like capillaries, but, as the vessels are much larger than ordinary capillaries, the walls are thicker; there is, however, no division into three coats. The two blood-vessels which are shown in the lung-tissue are probably of the same nature as those in the pleura. The lung-tissue itself is denser than normal, owing to the inflammatory hyperplasia. These new blood-vessels are of the same type as most of those shown by Fig. 21, and are typical of the ordinary new blood-vessels of hyperplasias. It is quite common to find the pleura thickened in various kinds of acute and chronic disease, and very often there are hardly any blood-vessels in the thickened diseased tissue. The fact that the envelopes of the thoracic and abdominal viscera and the portions of these organs near the surface are more often diseased than their deeper portions is a very curious one, and one that has as yet received no explanation.

FIG. 21.—NEW BLOOD-VESSELS IN LUNG AND IN PLEURA. (× 50.)

From a negro man forty-nine years old who died of Bright's disease. *d* is directly above a cross-section of a thick-walled blood-vessel, of which the opening is not centrally placed, and which is lined by a thin layer of endothelium containing rounded nuclei which look like beads. The free edge of the lung is thickened, being composed of fibrocellular tissue, and the pleura is bound to the lung, so that no distinction between pleura and lung can be seen. In this tissue there are many blood-vessels which are cut in various directions, and which contain red blood-corpuscles. Most of these are new blood-vessels.

FIG. 22.—NEW BLOOD-VESSELS IN THICKENED PLEURA AND IN LUNG. (× 50.)

From a negro man twenty-four years old who died of acute phthisis pulmonalis. *d* is the free edge of the pleura and *e* marks the line of junction of the thickened pleura and the lung. In the thickened pleura there are numerous blood-vessels which contain red blood-corpuscles, and in the lung-tissue there are similar vessels. All of these vessels have walls of fibrous tissue like very large capillaries, none of them being provided with three coats as arteries and veins are. The blood-vessels are a new growth resulting from disease.

FIG. 21.

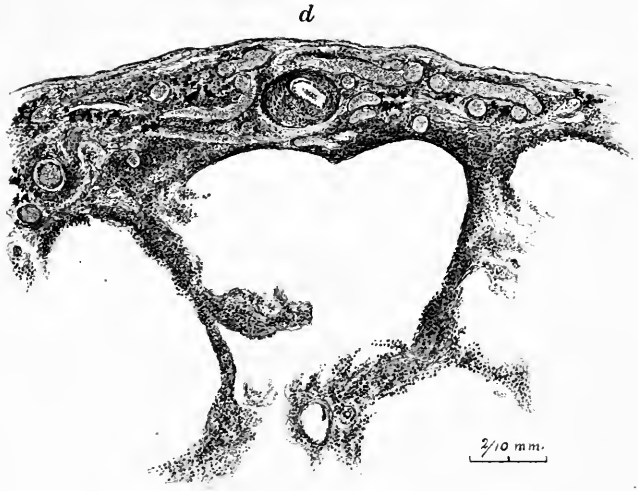


FIG. 22.

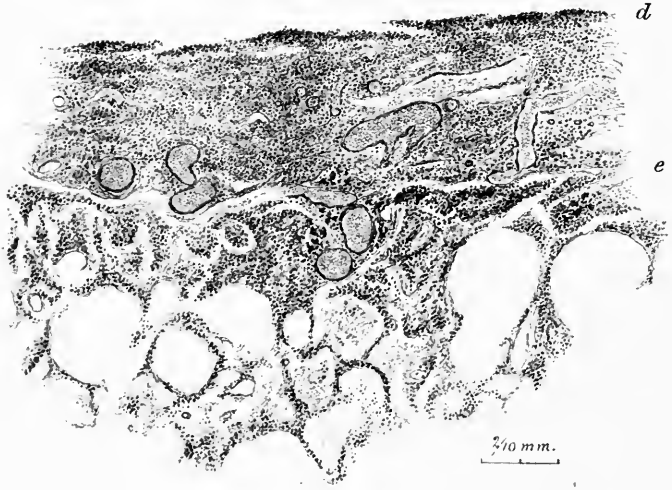


Fig. 23 depicts a portion of the thickened pleura and diseased lung of a negro woman seventy years old who died of Bright's disease. The pleura is many times the normal thickness, and the lung-tissue, instead of being of open texture like normal lung, is composed of a dense fibrocellular tissue containing pigment. The purpose of the drawing, however, is to show the new blood-vessels. There are several in the dense lung-tissue near the pleura and one which extends from the lung-tissue into the thickened pleura. In the normal state there are few if any blood-vessels extending into the pleura from the lung, certainly none of such great size as this one. The existence of this vessel is another exemplification of how nature provides a new blood supply whenever there is any hyperplasia like this thickening of the pleura.

Figs. 21, 22, and 23 demonstrate a peculiarity of disease which I have elsewhere discussed at considerable length,[1] but to which allusion may now be made. Fig. 21 depicts lung-tissue from a man of forty-nine, and Fig. 23 from a woman of seventy, and both died of Bright's disease. Fig. 22 shows pulmonary tissue from a man twenty-four years old who died of phthisis pulmonalis. Of the two who died of Bright's disease one was past middle life and the other was old, but the man who died of phthisis was still young. Although the ages were so different and the diseases so unrelated, there is a general similarity of the effects produced upon the tissue. Morbid fibroid tissue grew in the lung, and fibroid tissue of that character contains a greater or a less number of demonstrable cells, according to the rate of growth. In disease which has proceeded rapidly there are many cells in the diseased tissue, and in chronic disease dense fibrous tissue is produced which contains but few cells. This morbid fibrosis, or disease of age as I have elsewhere described it, is inevitable in human beings as they grow older, and is often produced in the young by disease when they fall into the condition of premature age.

The most dissimilar diseases produce the same change of the tissues, and it is very nearly correct to say that every kind of disease tends to cause the production of morbid fibroid tissue. A curious clinical fact is that the appearance of symptoms denoting the presence of disease in man has been preceded, for a long time perhaps, by the

[1] The Origin of Disease, Chapter II.

latent growth of morbid fibroid tissue in the body. Fig. 24 shows the spleen of a negro woman of seventy years who died of Bright's disease, the same patient from whom Fig. 23 was obtained, and, therefore, it might well be expected that there would be morbid fibroid tissue present, as morbid fibrosis is a disease which is apt to be widespread in the tissues of those who have it, especially in the aged. The splenic tissue does not appear to be abnormal; the capsule, however, is exceedingly thick and is composed of at least three layers of different tissues. As these are shown by the drawing, the old normal capsule is below, and next above it is new material the result of hyperplastic growth. Above this is still another tissue which is rich in cells and which contains a number of good-sized new blood-vessels. There are some small new blood-vessels in the middle layer of the capsule also. The uppermost layer of the capsule was evidently of rather recent growth, for old tissues are usually more densely fibrous and less rich in cells, and it probably constituted a portion of an adhesion by which the spleen was fixed to some adjacent structure, for in this case the abdominal viscera were almost all adherent to one another and to the surrounding parts. Such adhesions are very common in cases of chronic maladies, and especially in Bright's disease. When the capsule of the spleen is diseased as the result of a chronic process, it is prone to become thick and dense, sometimes of a texture almost like horn, and contains but few blood-vessels, but when the disease has been of rapid progress there are many new vessels. The appearance shown by Fig. 24 is very common in chronic disorders and in aged persons, and the production of new blood-vessels is an invariable part of the change.

In the lung, in cases of tuberculosis, it is quite common to find certain curious formations which have been named giant cells. Giant cells are also frequently found in the liver, spleen, and kidney and in other tissues. At one time they were thought to be peculiar to tuberculosis, and their discovery in any tissue was considered a certain indication of the existence of tubercular disease. It has been proved, however, that they exist in non-tubercular tissue. They develop, for instance, in granulation tissue. It is difficult to comprehend how they came to be called giant cells. Evidently in their full state of development they are not cells at all, but are complex formations composed of many cells. The general structure of giant cells and of the cells

FIG. 23.—NEW BLOOD-VESSELS OF THE LUNG. (× 50.)

From a negro woman seventy years old who died of Bright's disease. *d* is the free surface of the pleura and *e* the line of junction of the pleura and lung. The pleura is composed of coarse fibrous tissue and is greatly thickened. There is a new blood-vessel passing from the lung into the thickened pleura. The vessel, although of good size, has a wall composed of tissue like that of ordinary capillaries, but thicker than that of the smaller capillaries. There is no muscular tissue in it. There are a number of other blood-vessels in the lung-tissue which are filled with blood-corpuscles. These do not look like the normal blood-vessels of the lung.

FIG. 24.—NEW BLOOD-VESSELS IN NEW TISSUE. (× 105.)

A section of spleen, including the capsule and superimposed new tissue, from a negro woman seventy years old who died of Bright's disease. *h*, splenic pulp; *c*, true capsule; *g*, morbid tissue superimposed upon the capsule; *u*, the uppermost layer of the new tissue. It contains the new blood-vessels and many cells such as are commonly found in new and rapidly growing tissues. The vessel walls are formed of simple fibrous tissue, there being no differentiation into three coats and no muscular tissue. New blood-vessels are generally of this character. The tissue in which these vessels lie is probably a portion of one of the adhesions by which the spleen was fixed to adjacent parts.

FIG. 23.

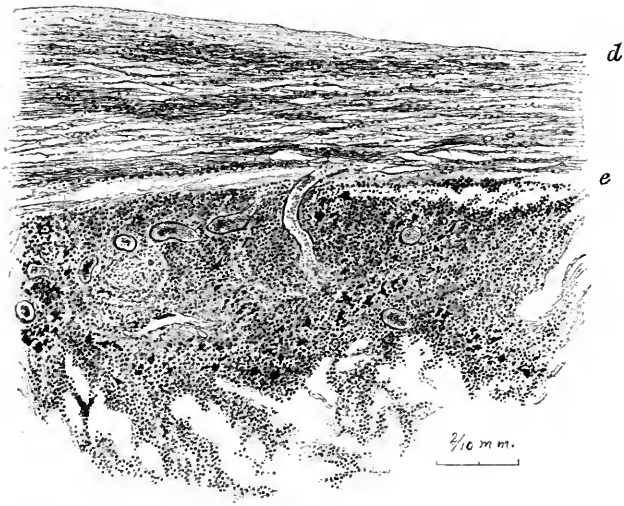
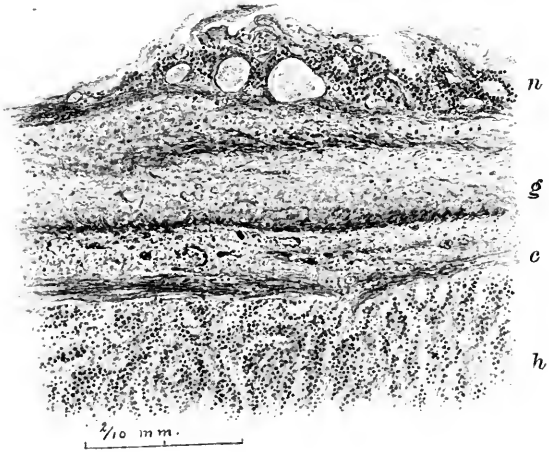


FIG. 24.



of which they are formed can easily be seen and studied with the microscope. The size of a well-formed giant cell is so great as at once to show the impropriety of calling it a cell. No cell of the human organism has ever been known to attain to anything like the size of a large giant cell. In view of the inherent tendency of nature to produce new blood-vessels in all hyperplasias, it is only reasonable to think they sometimes grow in tubercles, and I believe that giant cells are the result of nature's effort to form new blood-vessels. Some authorities have suggested that giant cells in tubercles are blood-vessels whose calibres have been obliterated by the disease. I think it is more likely they are caused by abortive attempts to produce new blood-vessels than that they are old vessels which were destroyed. A comparison of various forms of giant cells with new blood-vessels shows that in many respects they resemble each other.

Figs. 15 and 21, from "The Origin of Disease," depict deformed or aborted new blood-vessels. Many of the cells that compose these vessels are like epithelium and they bear little resemblance to the cells of normal blood-vessels. In two of the three vessels the opening is very small and is not central, and in the third there is no calibre, the aborted vessel being a solid cylinder. These illustrations seem to me to prove that the start to produce new blood-vessels in diseased tissues is sometimes made and fails, the cells growing exuberantly and irregularly, and that solid cylinders or odd-shaped forms are produced that are quite useless. Giant cells present many points of resemblance to these aborted new blood-vessels, as will presently be shown.

Authorities seem to agree that tubercles are non-vascular and that owing to this peculiarity they always break down as soon as they attain great size. The opinion of Ziegler has already been quoted, that "the formation of new blood-vessels plays a chief part in hyperplasias of every kind." Pathological studies show that when any new growth arises there is a strong tendency on the part of nature at once to provide a supply of blood, and tubercular disease certainly often partakes of the nature of a hyperplasia, for tuberculous lungs frequently are much larger and heavier than normal. If such be nature's law it would be strange if the only exception to it were in the case of tubercles. The statement that tubercles are completely non-vascular is not literally true. Probably what is meant by those who say that tubercles are non-vascular is that new blood-vessels do not develop in

them; but no one would assert that the blood-vessels in a tissue which is invaded by tubercular disease do not continue to exist for a time after the disease has begun. It must be, therefore, that tubercles are supplied with blood during their earlier stages, until there has been time to shut off the normal vessels. I have a number of specimens of tubercular disease of the lung of which the vessels were injected, and they show in the most satisfactory manner that there are many blood-vessels in the tubercles. In lung tubercles which are uninjected it is also easy to recognize blood-vessels within the tubercles. Such blood-vessels, however, commonly give the impression that they were in process of extinction, owing to the cellular infiltration and increasing density of the tissue, rather than that they are new or are developing.

The tubercular process in the human lung is subject to wide variation. Sometimes it is rapid, and in other cases very slow in its progress, lasting even for years. In rapid pulmonary tuberculosis the effect produced is exactly similar to what happens in cases of miliary abscess, so that often even a skilled observer cannot from a microscopical examination alone distinguish the one disease from the other at their beginning, although in their full states of development they are so far apart that it is then difficult to believe there was ever any resemblance between them. In rapid tuberculosis the cellular infiltration is overwhelming and the process is destructive from the first. The blood-vessels in the invaded tissue are soon cut off and destroyed. There is every reason to believe that in this form of tuberculosis there is not time for the formation of new blood-vessels. In disease of this nature few or no giant cells are found. When pulmonary tuberculosis has progressed more slowly, the effect is very different. Besides the infiltration with round cells a great quantity of fibrous tissue is produced which is well organized and is supplied with blood-vessels. It is in this tubercular tissue of slower growth that giant cells are generally found to be numerous and well developed. Such giant cells often present peculiarities of form and character which suggest that they are aborted blood-vessels. If giant cells are, as I believe, aborted new blood-vessels, the fact constitutes proof that new blood-vessels grow in the tissues of adults independently of the general vascular system, as they are known to grow in embryos, as I have already in this chapter tried to show. The prevalent disbelief in the indepen-

dent growth of new blood-vessels in diseased tissues and the opinion that they are always offshoots from pre-existing vessels stand in the way of the acceptance of the theory that giant cells are aborted blood-vessels.

Fig. 25 shows a number of giant cells from the lung, liver, and spleen. Some of them are from a man sixty years old who died of phthisis, and the others are from a woman twenty-five years old who died of meningitis and pulmonary tuberculosis. The description of the plate gives the details in regard to each one of the giant cells. These assume a great variety of forms and their appearance indicates that they are disposed to be irregularly cylindrical or oblong. Almost all of them have a fringe of cells forming an outer layer, while their central portions consist of a structureless, grumous-looking material. According to their relation to the plane of section they appear as circular, irregularly elliptical, or oblong. The fringe of cells forming the outer layer of most giant cells is incomplete (*g*, *i*, *j*, and *l*), but sometimes the cells are disposed in a complete circle (*c*, *k*). In one figure (*k*) there are two giant cells which are attached, by prolongations of the cells which form the external rings, to a blood-vessel which is close to them. The vessel is full of blood-corpuscles, and the intimate attachment to it of the giant cells suggests that they had some relation to the vascular system. The appearances of some of the giant cells (*a*, *d*, *e*, *f*, and *m*) strongly suggest that they are due to nature's abortive efforts to produce new blood-vessels in hyperplastic tissue. They appear to be solid cylinders which were cut in various directions. Some of them (*a*, *e*, *f*) suggest very strongly by their appearance that they are partially hollow cylinders, or that they were in process of becoming tubular. This effect has been very faithfully represented by the artist, and it is not exaggerated in the drawings.

The formation of giant cells in tubercles is a very common feature of tuberculosis, and there must be some explanation for the constant growth of these peculiar bodies. To call them giant cells is a misnomer, for evidently they are not cells but are complex bodies formed of cells. If they are not cells, what are they? Blood-vessels exist everywhere in the soft tissues, and blood-vessels grow in all hyperplasias unless tubercles form the single exception to an otherwise universal rule. Although it is impossible from existing evidence to prove that giant cells are deformed or abortive new blood-vessels, I believe

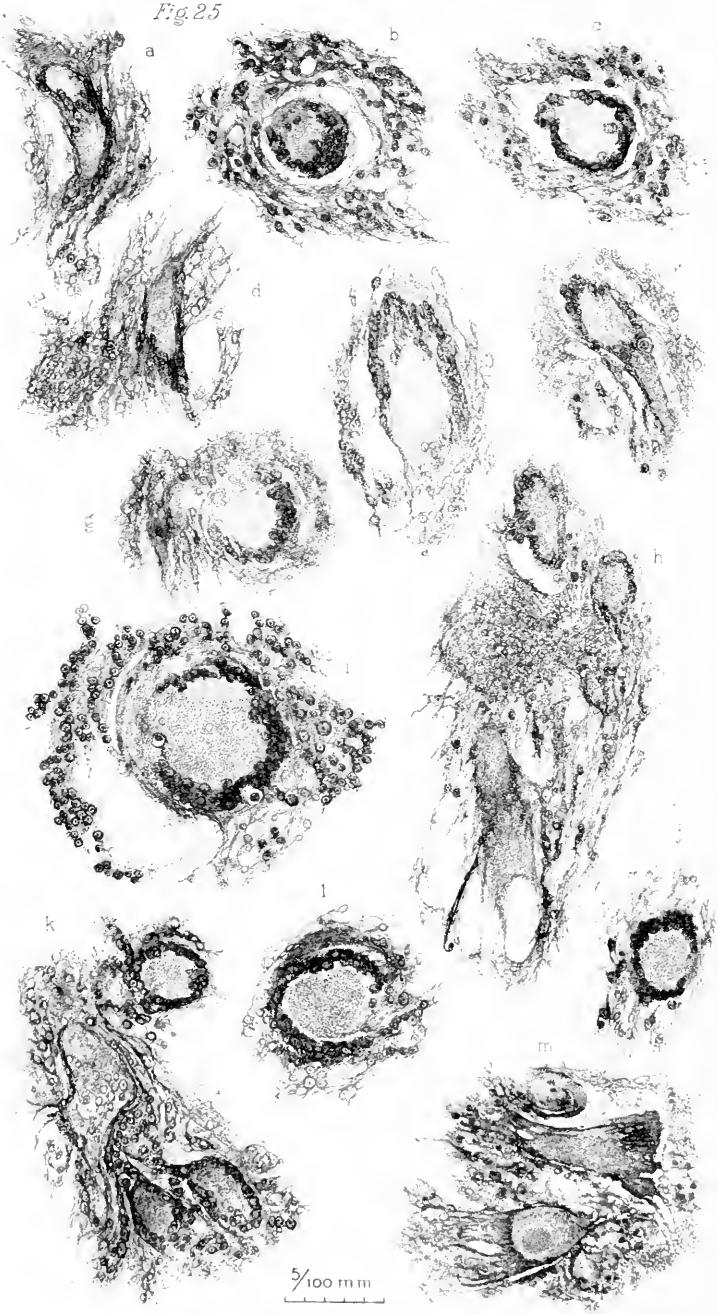
it is much more reasonable to accept such an explanation of their occurrence as a working hypothesis than to call them cells.

All of the foregoing discussion of new blood-vessels is, I am aware, imperfect, but the whole subject is at present in an unsatisfactory state and the information in regard to it that can be found in medical literature is very incomplete.

FIG. 25.—GIANT-CELLS. (× 260.)

a shows liver of a man sixty years old who died of phthisis. The giant-cell is cylindrical and was cut across at its upper end. It looks like a tube. *b* is lung from the same case as *a*. The giant-cell is nearly circular, has an almost complete outer fringe of cells, and is surrounded by an empty space, except at the upper left-hand portion, where a peduncle attaches the giant-cell to the lung-tissue. *c* is lung from the same case as *a*. The giant-cell is nearly round, except for an irregular projection to the left. Its outer border of cells is complete and the centre is composed of material without definite structure. It is surrounded by a space. *d* is liver from the same case as *a*. The giant cell looks like a cylinder that had been cut obliquely across, and the appearance suggests that it may have been a tube. *e* is liver from the same case as *a*. The giant-cell is partly separated from the surrounding tissue by a space. The arrangement of the cells at its sides and above makes it look as if obliquely cut, and as if it were hollow or partly hollow. *f* is liver from the same case as *a*. The giant-cell consists of an obliquely cut ring of cells with a projection below. It is like a cylinder or a tube. *g* is liver from the same case as *a*. The outer ring of cells is incomplete, which is a very common feature of giant-cells. *h* is liver from the same case as *a*. There are two giant-cells above which consist of incomplete rings of cells of irregular shape. Below these is fibrocellular lung-tissue, and at the lower part of the drawing is a giant-cell which is irregularly cylindrical, and has at its upper portion an irregular and almost shadowy ring of cells. This looks like an obliquely cut tube or cylinder. *i* is spleen of a woman twenty-five years old who died of meningitis and pulmonary tuberculosis. The giant-cell is formed of an incomplete ring of cells with structureless material in the centre. *j* is lung from the same case as *i*, to which it is very similar but smaller. *k* is lung from the same case as *i*. There are three giant-cells, one above and two below, and there is a small blood-vessel, containing corpuscles, in the middle. The giant-cell above is a common type. The two below appear to have been cut obliquely, and from the outer fringe of cells there is an extension attaching each of them to the adjacent blood-vessel. *l* is lung from the same case as *i*. This giant-cell is very like *i* and *j*, and is midway between them in size. In all of the three the encircling ring of cells is incomplete. *m* is spleen from the same case as *a*. There are two giant-cells which are of irregular shape. A study of all of the giant-cells makes it obvious that they are miscalled cells, and that they are complex formations of considerable size. They were all accurately drawn to scale.

Fig. 25



CHAPTER IV

Disease of Blood-Vessels in General

It is more satisfactory to study disease of the blood-vessels than disease of the large organs, for the largest blood-vessels are small in comparison with the great organs; and, as no study of disease is complete without microscopical examination, which can be made only with small masses of tissue, the reason why the study of blood-vessels is satisfactory is obvious. Complete cross-sections of the largest human blood-vessels can easily be prepared for examination with the highest powers of the microscope, and the study of a section across a blood-vessel is in a certain sense complete. If large organs like the brain or liver or even the kidney are to be examined microscopically for disease, it is feasible to select only such portions as can be seen with the naked eye to be diseased, and then to pick out haphazard other portions. It is impracticable to make a microscopical examination of the whole of one of the large organs, and, as disease sufficient to impair the usefulness of an organ is often quite invisible to the unaided eye, it must frequently happen that a grave malady escapes detection.

There is less known of disease of the capillaries than of disorders either of the arteries or of the veins, and the pathology of the veins has been less extensively studied than that of the arteries. This is true notwithstanding the fact that many of the veins lie upon the surface of the body so that the morbid changes they undergo are readily perceived. Varicose veins, for instance, are very common, and the condition has long been known and causes a great deal of suffering and disability, but its causes are little understood. Not much has yet been learned of the physical changes that occur in the veins themselves owing to disease. On the other hand, the objective study of the pathology of the arteries has been pursued to great length and a large store of facts has been accumulated. Although many of the morbid changes in the walls of arteries are well known, there is as yet no satisfactory understanding of the ulterior results of these alterations if the arteries themselves continue patulous and are thus able still to accomplish their most important function of carrying blood. It has

been neccessary to abandon many opinions formerly prevalent in regard to arterial disease. For example, endarteritis was at one time supposed to be due in most instances to syphilis, and it was thought to be possible from a microscopical examination alone to determine whether a lesion was of syphilitic origin. It is, however, now well known that endarteritis is one of the commonest vascular changes that take place in elderly people, that it is due to other causes much more frequently than to syphilis, and that it is impossible to ascertain from the appearances alone whether in a particular case of endarteritis the lesion is syphilitic.

Very little is yet known of the effects of changes of the anatomical constitution of the walls of the arteries and veins, although much care has been bestowed upon the study of the different coats of the arteries and elaborate theories have been evolved regarding diseases of the intima, the muscularis, and the adventitia, and as to perivascular disease. Increased experience has convinced me that pathological changes in the perivascular tissue and the adventitia of the arteries and veins are much more common than I formerly believed. It is always difficult in dealing with this subject to separate in a satisfactory manner perivascular disease from disease of the fibrous coat of arteries and veins. The distinction is of importance, for upon it turns the decision of the question whether in a particular case the malady is of vascular origin or arose outside in the connective tissue. It is possible for disease to begin in blood-vessels and then by extension to involve surrounding parts, or it may have its origin outside the blood-vessels and later include them by extension as it spreads itself over a larger area.

On some accounts anatomical and pathological classifications would be more satisfactory, and I believe more truly descriptive of nature, if arteries and veins were said to have only two coats—the muscularis and the intima—and the fibrous coat were classified as belonging to the perivascular connective tissue. It is always impossible to decide just how much of the fibrous tissue surrounding it belongs to an artery or to a vein and how much is perivascular connective tissue. If a large artery or vein be dissected from the tissue in which it lies, there is always a question how much fibrous tissue should be brought away as belonging to the adventitia of the vessel. In the same way, if arteries or veins are examined with the microscope in sections which

have been cut without disturbing the relations of the vessels and the surrounding tissue, a distinction cannot be made between the fibrous coat of the vessel and the fibrous tissue in which it lies. There is no line of demarcation between them, for the one shades imperceptibly into the other. All classifications are artificial, for they all draw hard lines and nature draws none. The more I have studied the subject of classification the more I am convinced that arteries and veins should be considered to have but two coats, muscularis and intima, as stated above. Gull and Sutton, in their description of arterio-capillary fibrosis which has become one of the classics of medicine, were the first to make known the important rôle which is played by the blood-vessels in most of the chronic diseases. It is impossible, however, even after the lapse of so many years, to be certain whether the disease which was the basis from which their conclusions were drawn—namely, fibrosis of the kidney—is truly of vascular origin or begins in some other portion of the renal tissue and secondarily produces its effects upon the blood-vessels.

The muscular coat of arteries is often greatly thickened and this thickening has been called hypertrophy, and the disease has been made the foundation for elaborate theories, it being said that the walls of the thickened vessels acquire a great increase of strength, and by their power of contraction check the circulation, reducing the amount of blood supplied to parts to which it flows through such arteries. The function of the muscular coat of the arteries and veins is not so well understood as it is to be hoped that it some day will be. Whether the contractility with which the muscularis is endowed has only to do with regulating the intravascular pressure, or if it furnishes part of the force which drives the blood onward, or if its function is something which has as yet entirely eluded observation, is a question for the physiology of the future to answer. This statement may be thought to be rash, but it certainly is true that the function of the muscular coat is not known in the same way that it is known that the contraction of the heart muscle drives the blood through the vessels. My own studies of the muscularis of arteries and veins have not yet led me to the discovery of a law governing the relative frequency of disease of it and of the other two coats, but I believe the intima to be the most subject of the three coats to disease, the muscularis to occupy the second place, and that disease of the adventitia

is the most rare. Morbid thickening of the muscularis is very common and is easily recognized. The question what is the nature of the tissue seen when such a thickened muscularis is examined with the higher powers of the microscope is a very different one, and one much more difficult to answer. There can be no doubt that in such tissue the number of muscle cells is increased, and this renders it almost certain that the actual amount of muscular tissue is increased; but it is my opinion, after having studied a great many diseased arteries and a large number of diseased veins, that this statement tells only half the story. If the so-called hypertrophied muscular tissue be carefully examined, it becomes evident that there are in it nuclei of a different character from the muscular nuclei, and that in many instances the muscular nuclei and threads of muscular tissue are more widely separated than in the healthy involuntary muscle of the blood-vessels. In some instances the nature of the material which separates the muscular elements cannot be determined, although even in such cases it is evident that the tissue is not wholly made up by an increase of the muscular tissue, but in others it is possible to recognize with certainty that connective tissue has grown among the muscle nuclei and fibres. As I have studied this so-called hypertrophy of the muscular tissue of the blood-vessels, I have been irresistibly driven to the conclusion that the process is a degenerative one. Quite frequently it is possible to see, in sections of arteries of which the muscular coat is thickened, that the thickened tissue is in a condition of fibroid degeneration, and it is impossible to believe that such tissue could have endowed the artery with increased contractile power. Incidentally it may be said that I have reached a similar conclusion in regard to hypertrophy of the heart,—that it is a degenerative process, and is not compensatory as it is commonly described to be.[1]

The question what causes the great increase of the bulk and weight of the human heart that often occurs in disease, and in an exactly analogous way of the muscular coat of arteries and veins, is an important one, and one therefore worthy of careful consideration. The belief that this strange process, which has been named hypertrophy, is compensatory and beneficial, is, I believe, without substantial foundation in fact. The theory has been generally accepted that

[1] Origin of Disease, page 84.

hypertrophy of the heart is nature's effort to overcome the ill effects of leaking of the valves, but the disease is known in its later stages to be degenerative and to be a cause of weakness. There is no good reason that I have ever been able to discover for the assertion that hypertrophy of the heart or of the muscularis of arteries and veins is compensatory at any stage of its development. Thickening of the muscular coat of the arteries and veins of any organ or tissue may occur. For instance, although disease of the intima is the most common lesion of the blood-vessels of the heart and kidney, it is quite common to find that the muscularis also is affected, and even that there may be morbid thickening of the muscularis of vessels that show little or no change of the intima. The artery in which I have most frequently found morbid thickening of the muscular coat is the radial. A common disease of the radial artery consists in a great thickening of the muscularis while the intima is but little thickened. The thickening of the muscularis is often so great that the disease is easily recognized by even the most casual examination. Such thickening I believe, as I have already said, to be due to degenerative growth and changes, and not to compensatory hypertrophy as has commonly been thought.

As yet I have been unable to discover the reason why the radial artery should be so very liable to thickening of the muscularis, which is a disease so different from that which is most common in the arteries of the organs and especially of the heart and kidneys,—namely, thickening and degeneration of the intima. It may be that the blood-vessels within the organs are less subject to disease of the muscularis than are the arterial trunks which carry the blood to the various parts of the system. Such examinations of arteries as I have made seem to support this view, for in the femoral, popliteal, brachial, etc., the muscularis has appeared to be proportionally more frequently diseased than in the arterioles which are within such organs as the heart, spleen, and kidneys. It appears that the blood-vessels of the organs are more liable to have the intima first attacked by disease than are the vessels which serve as trunks to carry the blood from part to part. Many of the great vessels, both arteries and veins, are but little supported by surrounding solid tissue in their course from the heart, which is the centre of the circulation, to the part of the organism to which they supply blood. The vascular

trunks of the thorax and abdomen, as well as those of other parts of the body, are like the pipes of a system for a water supply, which in their transit are hung in spaces without having anything around them. On the other hand, the blood-vessels of the organs are surrounded by tissue which is more or less dense and from which, in the nature of things, they must receive support. It is not surprising that blood-vessels whose environment is so very different should be anatomically as different as the great vascular trunks are from the vessels within the organs, nor would it be surprising if the event should show that they are different in their liability to become diseased. Owing to their activity and to their important functions, the organs are more subject to disease than are the spaces and side ways through which the vascular trunks pass and in which they are suspended like pipes. Disease of the intima is a characteristic of the arteries and veins of the organs, while, on the other hand, there is a good deal of evidence tending to show that the vascular trunks occupied in carrying the blood are more subject to primary disease of the muscularis.

Figs. 26 and 27 represent a small fusiform aneurism of the subclavian artery, which pulsated violently during the life of the patient. There are thickening of and calcareous deposit in the muscularis of the artery. It is strange that there is not more evidence of disease, for the pulsation of the artery was always very violent and the patient was under observation for several years and died of an intercurrent malady. Fig. 26 demonstrates little except that the wall of the artery is of uneven thickness. Fig. 27 shows the muscular tissue to be more open meshed than is natural, and calcareous material can be seen lying between the threads of muscular tissue. The muscular coat is thickened, but it would certainly be unreasonable to suppose that such diseased tissue was endowed with an increase of power to contract. The calcareous deposit which is scattered in small particles through the arterial wall lies in the muscular tissue. This is an interesting and instructive fact, because it has been said by some authorities that chalk is generally first deposited in the plicated membrane. The plicated membrane is a striking feature of the appearance of most middle-sized and small arteries. In properly prepared sections of normal arteries it is easily seen, and it constitutes an important landmark, for it sharply separates the muscularis from the intima. It

FIG. 26.—ANEURISM. (× 8.)

From a woman forty-seven years old who died of obstruction of the bowel. The section is through a small aneurism of the right subclavian artery. It shrunk a good deal after death. Much of the tissue stained badly and the lining of the artery is loose; this is perhaps a post-mortem change. *h* indicates an area represented more highly magnified by Fig. 27.

FIG. 27.—ANEURISM. (× 50.)

The region indicated by *h* in Fig. 26. The three coats cannot so easily be distinguished as they generally can be in small arteries. The appearance approaches more nearly to that of the aorta, in which there is never a distinct plicated membrane separating the intima and muscularis. *i*, intima; *m*, muscularis; and *a*, adventitia. *c* indicates a deposit of chalk. The muscularis is loose-meshed, and there is less muscular tissue than is natural, and a good deal of chalk can be seen deposited between the muscle-fibres.

FIG. 26.

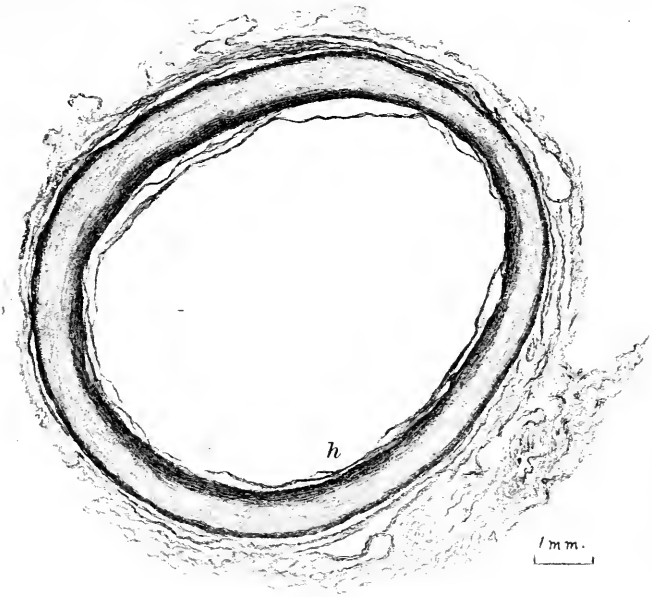
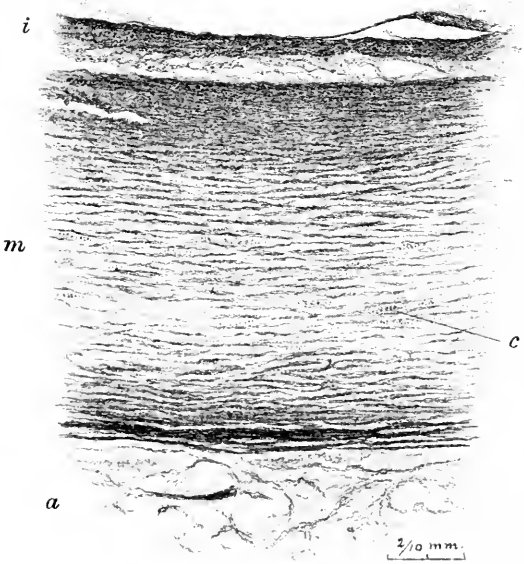


FIG. 27.



is considered to be a part of the intima, but I am not able to comprehend why this should be. There is much elastic tissue scattered through the muscularis and very little in the intima of arteries, and this seems a reason why the plicated membrane might more reasonably be considered to belong to the muscular coat than to the intima. The question to which of the three tunics the plicated membrane properly belongs, or if it has a separate existence of its own, is not easy to answer. The fact that this question of anatomical classification cannot at present be answered, need not, however, interfere with the progress of pathology, for not knowing exactly how to classify the membrane will not interfere with the observation of its diseases. The statement has been made that calcareous degeneration of the arteries begins in the plicated membrane, but this position cannot be rigidly maintained. My own observations have shown me that chalk may be deposited in any part of a blood-vessel, and Fig. 27 demonstrates primary chalky deposit in the muscularis. Morbid deposits of chalk may occasionally be found in almost all parts of the body, and it would be strange if the chalk were always deposited first in the plicated membrane when the disease occurs in the blood-vessels. In examining sections of arteries I have found at different times chalky deposits in all three of the tunics, but most of the arteries that one has the opportunity to examine are those in which the disease has proceeded far and the deposits are extensive. Even if a section is obtained in which chalky deposit is found confined to the plicated membrane, it is impossible to know from the single section that the deposit is not a part of a large one which extends into the other coats. Under such circumstances it is not possible to ascertain in which tunic the disease originated. Fig. 28 confirms the correctness of this statement. It is one of a set of serial sections of the radial artery of an old man. Other sections of the series show that the deposit of chalk is much larger than it appears in Fig. 28 and that it extends far into the muscularis and intima, destroying large portions of them. Were it not that the other sections show that the spot of calcareous degeneration is such a large one, it might be thought that Fig. 28 confirms the view that calcareous degeneration begins in the plicated membrane, whereas it is not possible from study of it and of the rest of the series of sections to learn in which of the coats the chalk was first deposited. Incidentally it is inter-

esting that there are minute chalky deposits scattered through the muscularis of Fig. 28 which are exactly similar to those shown by Fig. 27. For some reason these are not shown by the illustration (Fig. 28).

In arteries of which the intima is thickened it is common for the plicated membrane to be destroyed, so that no trace of it can be seen at those parts at which the thickening of the intima is greatest. In other diseased arteries it is quite common to find that the plicated membrane has been completely destroyed. It presents many points of resemblance to the cornea of the eye, which in a natural condition appears to be structureless and without cells, but becomes opaque when inflamed. This process has been studied in the lower animals by irritating the cornea so as to cause inflammation. Disease which presents changes similar to those that arise in the cornea when it is irritated occur in the plicated membrane. I believe that these changes constitute one of the earliest if not the earliest form of chronic disease of the arteries. This subject is discussed in my book on the "Origin of Disease,"[1] and the illustrations show various stages of the disease. The plicated membrane, which in its healthy state is clear and glassy, becomes muddy and cells become distinguishable. As the process progresses its transparency is lost, and it is so much changed in character that it can no longer be recognized. The cellular tissue which is formed from the plicated membrane appears to become a part of the thickened intima. Although often thus destroyed and contributing a portion toward the formation of thickenings of the intima, it frequently happens that the intima is greatly thickened and diseased and yet the plicated membrane remains to form a distinct boundary separating the muscularis from the intima ("Origin of Disease," Figs. 10 and 11). The growth of cells in the plicated membrane and its destruction by being converted into a completely cellular tissue indistinguishable from the intima occur in chronic disease at all periods of life.

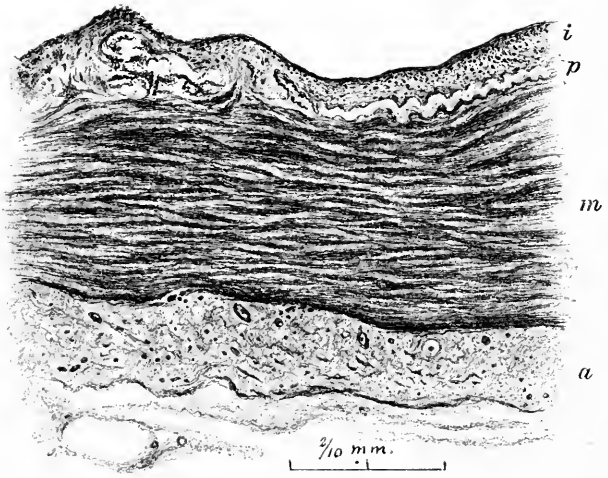
Disease of the intima is of more frequent occurrence than disease of the other vascular tunics, and the commonest form of it is the thickening which is called endarteritis. As syphilis used to be supposed to be the most frequent cause of endarteritis, it is necessary, as has

[1] Page 42 and Figs. 7, 8, 9, 10, and 11.

FIG. 28.—CALCAREOUS DEPOSIT IN THE RADIAL ARTERY. (× 105.)

A section of the radial artery of a man sixty years old who died of endocarditis and cardiac dilatation. *i*, intima; *p*, plicated membrane; *m*, muscularis; *a*, adventitia. Toward the left the plicated membrane enlarges and becomes obscured by the deposit of the chalk, which is distinctly shown.

FIG. 28.



already been pointed out, to remember that syphilitic endarteritis cannot be distinguished from endarteritis due to other causes. It should also be kept in mind that thickening of the intima of the arteries is the commonest change that takes place in the blood-vessels as life advances, and that it is of frequent occurrence in young persons and even in infancy in cases of chronic disease. The study of disease of the intima is made difficult at present by the fact that there is no accepted standard to establish what is a normal intima. In text-books of histology there are pictures and descriptions of the intima of various blood-vessels and of it in vessels of different sizes, but no account is taken of the fact that with the progress of years there is in all human beings a tendency for the intima to become thicker. This tendency is so universal that there cannot be any doubt of its existence. The lack of a standard of the normal makes it difficult in individual cases to decide whether a particular change of the intima that is being studied is really disease and was injurious, or if it is so slight that it must be regarded as merely the natural result of the passage of time and therefore harmless. This difficulty is very real to any one who has studied disease of the blood-vessels, and sometimes it is impossible to find a conclusive and satisfactory solution of it. The subject of the bodily changes incident to the advance of years I discussed in my book on the "Origin of Disease," and in the chapter on the "disease of age" I tried to demonstrate that such a thing as a physiological old age has no existence. The changes of the organs and of the tissues that come with advancing years are as real and as visible to the eye, if sought for, as the lesions which are due to any of the common diseases, and these physical changes inevitably attendant upon the increase of years necessarily weaken the individual, and in time, when they have progressed sufficiently far, they must cause death. It is, however, quite impossible to forecast the rate at which the changes due to age will progress.

Disease of the intima can hardly occur without causing some thickening of the vessel-wall and this thickening must reduce the calibre of the affected vessel. There is no escape from the conviction that reduction in size of its calibre must take away from a blood-vessel its state of physiological perfection. As men increase in years the intima of the arteries thickens as surely as the face becomes wrinkled and other changes occur which make it possible to distinguish an old man

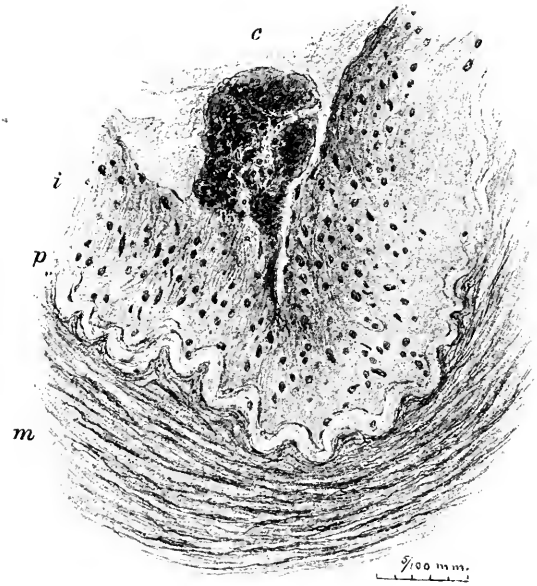
from a young one. Although this thickening of the intima must reduce the size of the calibres of the affected blood-vessels, it is not well to be hypercritical, and pathologists should not exaggerate its importance, for if moderate in degree there is every reason to think it harmless. At the same time there cannot be any doubt that the process is a disease. The lexicon of the New Sydenham Society defines disease as "a departure from the state of health, especially when caused by structural change." If this definition be accepted as correct, thickening of the intima of the arteries is a disease. Although there is every reason to believe that the disease in its lesser degrees does no appreciable harm, it is quite certain on the other hand that greatly narrowed arteries and veins cannot perform their functions in a perfect manner. The intima is often so thick that it alone is of greater diameter than the other two tunics together, and under such circumstances the vessel must lose efficiency both because of the reduction in the size of the opening and because its elasticity and its power of contractility are reduced. Almost all of the elastic tissue is in the muscularis and adventitia, and the freedom of motion of these two coats which surround the intima must be greatly reduced when the intima is morbidly thickened. Whatever service the elasticity and contractility of the blood-vessels may perform, the perfection of action must be interfered with by any great thickening of the intima.

Fig. 29 is a drawing of part of a section through the wall of the radial artery, and the intima and a portion of the muscularis are included. There is a clot inside the vessel which is attached to it by threads of tissue which penetrate quite deeply into the intima. The formation of clots within the blood-vessels is a disease process of importance, and it probably occurs frequently and at all periods of life. There is good reason to believe that the deposit of clots within the vessels sometimes contributes a part and perhaps a large part toward causing thickening of the intima. This subject is discussed in my book on the "Origin of Disease" (page 57). Fig. 29 shows thickening of the intima of moderate degree. The tissue is a good type of what is usually formed as a result of disease of this nature, and is quite unlike any of the normal human tissues. It is different from the ordinary forms of connective tissue and is more like epithelium than anything else, but is in some respects different from normal epithelium.

FIG. 29.—ORGANIZED CLOT ATTACHED TO THE INTIMA OF AN ARTERY. (× 240.)

From the same case as Figs. 36, 37, and 42,—a negro woman twenty-seven years old who died of typhoid fever. A section extending part way through the radial artery; the adventitia is not included and only part of the muscularis. The artery is not normal, for the intima is unnaturally thick. *m*, muscularis; *p*, plicated membrane; *i*, intima; *c*, clot, which contains cells that were living, and there are threads extending into the intima and attaching the clot to the lining of the artery.

FIG. 29.



There is probably no other disease of the blood-vessels which has been so extensively studied and so much discussed as atheroma. I have found the term somewhat differently defined in dictionaries. The best definition is that given by the Century Dictionary, and it is as follows: "1. A name given to various kinds of encysted tumors, the contents of which have the appearance of bread-sauce. 2. The formation of thickened patches of the inner coat of an artery (much more rarely of a vein), constituting flattened cavities which contain a pasty mass exhibiting fat-globules, fatty acid crystals, cholesterin, more or less calcareous matter, etc. The endothelial film separating this from the blood may give way, and an atheromatous ulcer be formed." The derivation of the term atheroma is from a Greek word meaning a gruel. It is evident from this that the term, as commonly used to designate the disease of the arteries to which it is applied, is employed in quite a different sense from its original one. The lexicon of the New Sydenham Society gives the original significance of the word atheroma and then says that the "term is also used alone to signify a different disease, atheroma of the arteries," and refers to "arteritis" for a detailed description. Under the head "arteritis" it describes various forms of atheroma of arteries, evidently meaning to convey the impression that all kinds of it are varieties of inflammation, although no direct statement to that effect is made. It has grown to be the custom of recent years to designate by the word atheroma most of the common changes of the lining of arteries which can be distinguished with the unaided eye and which occur also in the veins, but it has been supposed much less frequently. Under it are included abscesses, ulcers, thickenings, patches, and calcareous deposits,—in short, almost every change of the lining of blood-vessels which can be seen without the microscope. When the many forms of disease thus called atheroma, and which have been included under a single head, are studied microscopically, they are variously subdivided in accordance with the nature of their causes and formation. Most of them are the result of acute or chronic inflammation, if inflammation be accorded its broader and more comprehensive meaning. It is astonishing how little is known of the effects of these changes of the lining of the blood-vessels. It is not rare to see old men in the enjoyment of good health, with all the arteries near the surface tortuous and hard and the surface veins distended and rigid to the

touch, and, on the other hand, to find post mortem, in persons in whom there had not been the slightest clinical evidence to indicate the existence of such a thing, that the internal blood-vessels are greatly diseased. Although the economy is wonderfully tolerant at times of extensive vascular disease, there cannot be any doubt that disease of the blood-vessels does produce most important ill effects and that their state of well-being is necessary to good health. The fact that so little is known as yet of the effects of disease of the blood-vessels should make pathologists patient, and should encourage them to be willing to continue the objective study of vascular disease and to record its various appearances without expecting at present to be able to explain the effects of the lesions found. From the foregoing, it is evident that the word atheroma has been used in a somewhat loose sense, and that when precision of meaning is wanted the term is an unsatisfactory one.

One of the commonest causes of death in persons over fifty years of age is cerebral hemorrhage, and it is generally the result of disease of the intima of the arteries. I cannot express my views upon the subject better than by the following quotation from my book on the "Origin of Disease" (page 172): "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, where 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 belief which commonly prevails, that some physical effort, or a disturbance of function causing the heart to beat with unusual violence, is generally the immediate cause of apoplexy, is without foun-

dation. The hemorrhage results from an ulcerative process, which is generally of chronic rather than of acute character, and often is quite latent in its manner of progress. Although it is true that the ulceration of the vessels which is antecedent to cerebral hemorrhage is often latent, yet it is not always entirely so, for it is not rare that fatal apoplexy is preceded by certain symptoms which are well known to clinicians.

CHAPTER V

Disease of Veins

The information that can be obtained in regard to disease of the veins is meagre and is not precise; it is therefore unsatisfactory. What is known of the subject has been better formulated for the clinician than for the pathologist. It is possible to ascertain from text-books the gross pathological appearances usual in certain known diseases of the veins, but the pathological histology of disease of the veins has not been systematically recorded. A careful collection and a systematic record of what is known are very much to be desired, but the task of making such a collection and record is one I have not undertaken, and I shall not attempt more than to describe the peculiarities of veins that I have myself seen. In text-books there may be found descriptions of calcareous deposits in veins, of phlebitis, of endophlebitis, of hyperplastic phlebitis, and other diseases to which veins are subject, but the descriptions are incomplete. What I have learned of the diseases of veins, beyond reading such descriptions, has been gained almost entirely from post-mortem study, and not from the study of disease of veins during life.

In cases of fibrosis of the veins the appearances are most interesting and curious. Just as happens to the arteries, the veins are involved when the fibroid process is extensive, and in the case of the veins, as well as of the arteries, it is often impossible to decide whether the disease originated in the blood-vessels or outside of them and independently. The general subject of morbid fibrosis is a very large one and one of the utmost importance, but, as I have already discussed it at considerable length in my book on the "Origin of Disease" (page 9), it is unnecessary to repeat what is there included. Figs. 30 and 31 represent a curious form of fibroid disease of a vein. Fig. 30 shows a radial artery and the two veins. The artery is thick walled, but it presents no unusual features, and the condition will be described in the chapter on disease of radial arteries and veins. Fig. 31 is a more highly magnified view of the vein to the right in Fig. 30. The vein is thick walled, and it is easy to see that much of the increase of thickness is due to the growth of morbid fibroid tissue.

FIG. 30.—DISEASED RADIAL ARTERY AND VEINS. (× 20.)

From a negro woman of twenty-three who died of ulcerative endocarditis. The artery is in the centre and the veins are upon either side of it. The vein to the right is represented more highly magnified by Fig. 31. The three vessels are all thickened. They probably shrunk a good deal post mortem.

FIG. 31.—FIBROID DEGENERATION OF A VEIN. (× 105.)

A vein from Fig. 30 more highly magnified. There is a large clot in the lumen. *a*, adventitia; *m*, muscularis. It is loose-textured, instead of being a closely woven tissue, as normal involuntary muscle usually is. Between the darker strands of the muscular fibres is a light-colored tissue containing nuclei,—this is morbid fibroid tissue. *i*, intima, which has upon its inner surface a fringe of bead-like nuclei which lie in folds. This folding was probably caused by post-mortem shrinkage. *b*, a minute capillary; *f*, an area of fibroid deposit in which the nuclei are set across the circle formed by the wall of the vein. Near this region the muscular fibres are torn apart, and there is an opening through the strands of muscle just below the capillary *b*. It looks as if morbid fibroid tissue had invaded the muscularis of the vein from the perivascular connective tissue, just as cancer progresses by forcing its epithelioid cells into surrounding tissues.

FIG. 30.

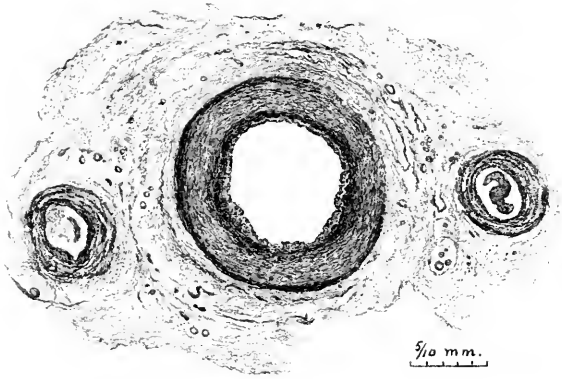
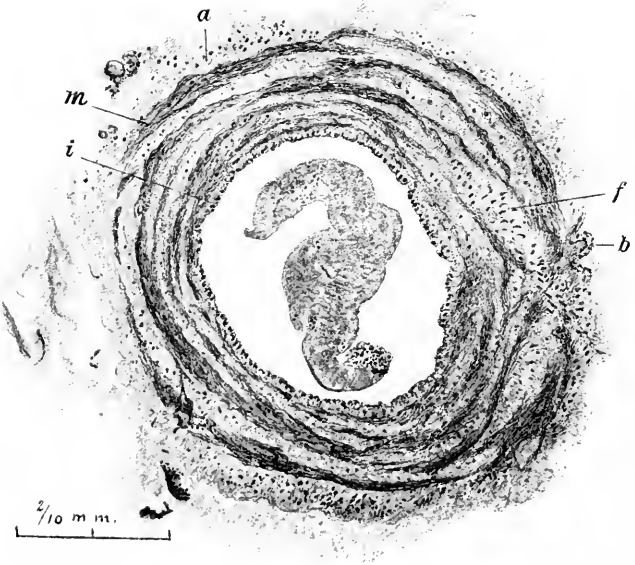


FIG. 31.



The adventitia, the muscularis, and the intima are easily distinguished. The adventitia presents no notable features and the intima is slightly thickened, but the muscularis is very thick and is much diseased. The muscular tissue is disposed in irregular bands of various sizes, and these are of different lengths, and the spaces between the strands of muscle are filled with fibrous tissue. It is quite unlike any natural involuntary muscular tissue and I have never seen similar disease of arteries. It looks as if the fibrous tissue of the adventitia or the perivascular fibrous tissue had insinuated itself into the muscularis of the vein and had torn and split the strands of muscle apart. To the right in the picture there is an opening in the muscularis in which many nuclei of fibroid tissue can be seen, and it seems as if this fibrous tissue had grown from the outside through the opening into the muscular tissue. The effect produced is very like that which is often seen at the margin of a cancer when the cells of the new growth force themselves into the surrounding tissue, overwhelming it and changing its character as the cancer extends. This appearance of a growing cancer at the margin is very familiar to those who have studied pathological histology. In the vein, Fig. 31, the line of separation of the muscularis from the adventitia is less sharply marked than in normal vessels. The outer boundary of the muscular coat is broken by openings in the muscle which are filled with fibrous tissue. There is, of course, no line of separation between adventitia and perivascular connective tissue. Fibroid disease of a vein of such a nature makes one think again of the enlightening essays of Gull and Sutton on arteriocapillary fibrosis. They did not make an exact demonstration, but their observations were the first to draw attention to the importance of the disease whose visible manifestation is morbid fibrosis. The disease fibrosis is not understood further than that it is recognized that there is a tendency sometimes for fibrous tissue to grow where it ought not and cannot without injury to the organs or tissues affected. This morbid tendency to the growth of fibroid tissue presents many points of resemblance to the malignant diseases cancer and sarcoma,[1] of the causes of which nothing is yet really known except that cancer is the result of the irregular growth of epithelium and sarcoma of the irregular growth of mesoblastic tissue. Many

[1] Origin of Disease, by Arthur V. Meigs, page 20.

pathologists think there is an extrinsic cause, but there is no reason for such a belief unless the fact that it is hard to understand how cancer and sarcoma could begin without an extrinsic cause be considered a reason. To assert the existence of an extrinsic cause because no other explanation is at hand is unscientific and is quite unwarranted. Morbid fibrosis is a disease of great importance, and it is to be hoped that more will be learned of its causes and effects.

Fig. 32 depicts a vein from the margin of an ulcer of the ankle which had thickened edges. It was removed by operation from the living patient. With the unaided eye it was seen that the vessel had thick walls and a very small opening. The disease was purely local and was thought to be due to sluggish inflammation or to syphilis. The illustration shows great fibroid thickening of the vein. It is difficult to recognize the three tunics, and their lines of separation from one another are quite lost. The intima is thickened and it is of unnatural appearance. Muscular tissue can be distinctly recognized, but the strands are separated so that it looks as if it had been torn and distorted like the muscular tissue of Fig. 31, but even more so, for the greater part of the tissue composing Fig. 32 is fibrous. There are minute blood-vessels in the adventitia and two or three nerve-fibres which were cut across. It seems impossible to explain the appearance except on the theory that the effect was produced by the growth of morbid fibroid tissue in the walls of a vein that was once normal. From the appearance only of this vessel it would be impossible to be certain that it was a vein and not an artery, but it was distinctly recognized to be a vein in the tissue of the living patient, and when cut contained venous blood. I have never myself seen an artery affected in a similar way, but am unable to say whether arteries ever are so diseased.

Fig. 33 represents an artery and a vein of the kidney. The section was cut without any disturbance of the natural arrangement of the parts; the two vessels are therefore surrounded by the kidney tissue just as they were during the life of the patient. A most curious form of fibrosis is exhibited by the two vessels. The artery is a type of the form of disease which most commonly affects the arteries of fibroid kidneys. The wall is thick and the calibre small. The intima is much thicker than is normal and is of irregu-

FIG. 32.—ENDOPHLEBITIS. (× 50.)

From a man of thirty-nine years. The vein was cut during life from the margin of an acute ulcer of the ankle. The ulcer had thickened raised edges. The wall of the vein is greatly thickened and the lumen a mere slit. Although the disease was acute, the changes are very like those shown by Figs. 34 and 35. In this case it is difficult to make a precise differentiation of the three coats. The tissue is loose-meshed and contains many nuclei, as is usual in rapidly growing structures.

FIG. 32.

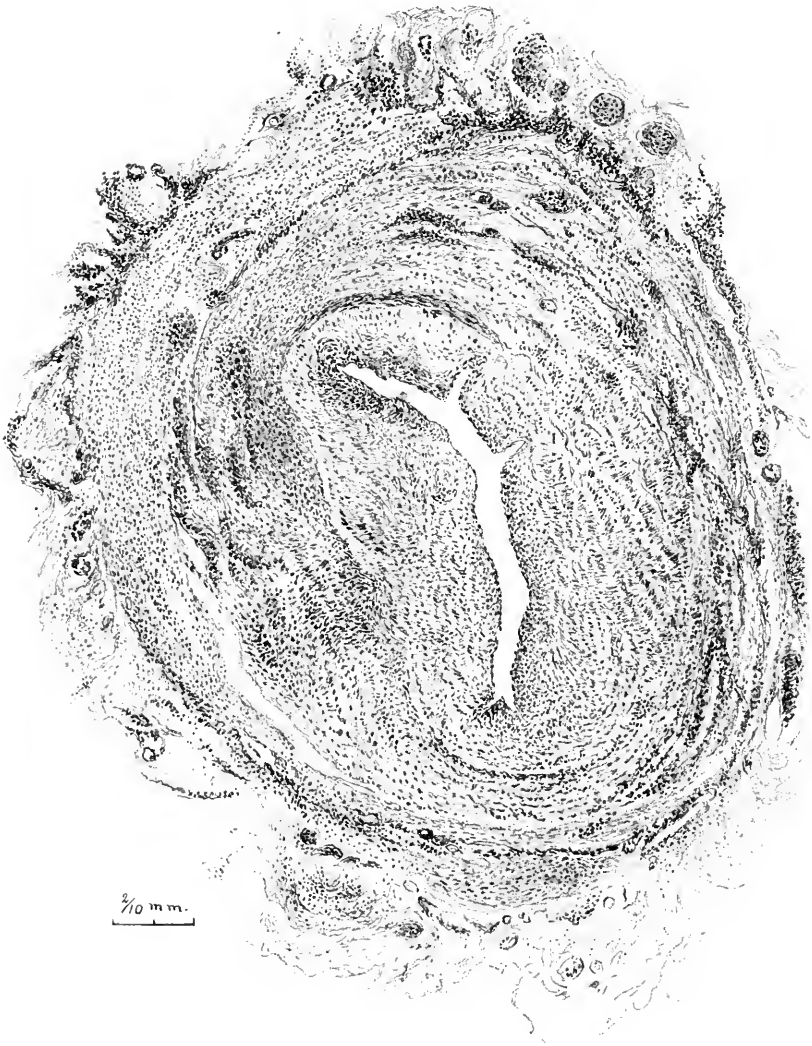
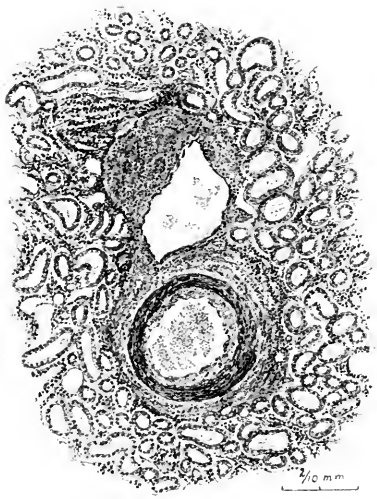


FIG. 33.—DISEASED ARTERY AND VEIN OF THE KIDNEY. (× 50.)

From a woman forty-seven years old who died of obstruction of the bowel. The kidney is fibroid and the blood-vessels lie in a fibroid area. The artery shows in typical form the thickening that is common in the kidney, which in this instance is of moderate degree. The intima is irregularly thickened and the muscularis also is a little thicker than normal. Outside the muscularis is the adventitia, which consists of fibroid tissue, and it is impossible to say where the adventitia ends and the perivascular connective tissue begins, for there is no line of separation. Above the artery is the vein, and its appearance is striking and very peculiar. Its wall is a ring of endothelium surrounded by fibrous tissue. There is no differentiation between the wall of the vein and the surrounding morbid fibrous tissue of the kidney. The vein must at one time have had a distinct wall with muscular tissue in it. Disease sometimes produces an effect like this in the spleen. See Fig. 92.

FIG. 33.



lar thickness at different parts. The muscularis is a little thicker than natural and is irregularly thick. The irregularity of thickness of the intima and muscularis is certainly abnormal. The adventitia and the perivascular connective tissue are absolutely indistinguishable, and therefore it is impossible to say whether or not the adventitia is thickened. The vein, as it is seen in cross-section, appears as a ring of endothelium surrounded by dense fibrous tissue. There is nothing to indicate that there ever were three coats. The fibrous tissue is not like the natural adventitia of blood-vessels, and it is continuous with the morbid fibroid tissue of the diseased kidney and with that around the artery. There is no line of separation of the adventitia of this artery and vein from the perivascular connective tissue surrounding them. They furnish, therefore, a good illustration to support the opinion that has been expressed (page 6) that blood-vessels should be described as having only two coats, the intima and the muscularis, and that the adventitia should be regarded as a part of the perivascular connective tissue. It is impossible from the study of blood-vessels like these two to decide whether the fibroid disease that they exhibit originated in them or in the surrounding tissue and later included them in the course of its extension. In this case the vein is much more diseased than the artery, for although the three tunics are thickened and diseased in the artery they are easily distinguishable because they retain their characteristic appearances, but the vein is a mere channel in fibrous tissue. It would be impossible to recognize it as a vein were it not for its situation beside the artery. The endothelial lining and the blood-corpuscles which lie within the calibre would not enable any one to be sure it is a vein. Blood-vessels so greatly changed as this vein is cannot be recognized except by their situation or by some other characteristic that remains unaltered by the disease. Veins and arteries become indistinguishable when greatly diseased. Although the walls of veins are usually thinner than those of arteries, it is not rare to find diseased veins with walls as thick as those of their accompanying arteries. Fig. 75 depicts such a vein and artery; but they are more fully described at page 87. Veins like this one are generally found to have undergone extensive fibroid infiltration of the muscularis.

Figs. 34 and 35 represent disease of a vein. The illustrations have

already been published.[1] They are drawings of the same vein, which was removed during life from the dorsum of the foot of a man twenty-five years old. Fig. 34 shows fibroid disease in many respects like that shown by Figs. 31 and 32, which has already been described. Fig. 35 exhibits another curious disease to which veins are subject—proliferation of the intima. This proliferation is sometimes extraordinarily great, and I have found it in the radial and in other veins as well as in this one. The intima grows so rapidly that its proliferation outstrips that of the other tunics, and it becomes separated from the muscularis and fills the lumen, so that when the vein is examined in cross-section the proliferated intima looks like a bundle of earthworms. There is not generally a distinct plicated membrane in veins, as there is in arteries; but the enormously proliferated and convoluted intima that is shown by the drawing is composed of a glassy and nearly homogeneous membrane with endothelial plates upon its edges, which is structurally like the plicated membrane as it is sometimes seen in arterioles in the earlier stages of endarteritis. I have never seen this excessive proliferation with convolution of the lining in an artery; but there is nothing at present known to explain why the disease should be peculiar to veins. The peculiarities of the vein which is shown by Figs. 34 and 35 are described and the clinical history of the patient, who was a man twenty-five years old, is given in the essay on endophlebitis which has already been cited. From that essay I shall quote:

"A small vein which extended across the right foot about an inch from the roots of the toes, and which received branches from the superficial veins of the toes, could be felt to be distinctly thickened. As this vein lay directly beneath the skin, its unnatural thickness could easily be distinguished by passing the finger back and forth across it, especially where it crossed the tendons, which made a firm background against which to press it. It felt like a minute cord, instead of almost disappearing when compressed, as a healthly vein will do when felt through the skin. The corresponding vein of the left foot also was much thicker than natural, but less than the one that has been described. As the patient said he was quite willing, a short incision

[1] Endophlebitis, by Arthur V. Meigs, Journal of Anatomy and Physiology, vol. xxxiv., July, 1890, page 458; and Transactions of the Pathological Society of Philadelphia, November 9, 1899.

FIG. 34.—DISEASED VEIN. (× 56.)

From the dorsum of the foot of a man of twenty-five years. Removed by operation. The vein is almost closed by thickening of the muscularis. The thickened muscularis is only partly composed of true muscular tissue, which has been torn apart and thrown into wavy strands by morbid fibroid tissue which has grown in it. *x*, the line of separation of the fibrous coat from the muscularis; *y*, the line of separation of the muscularis from the intima. All the tissue between *x* and *y* is muscularis; the thickening of it is very great. At *y* the separation of muscularis from intima is clearly marked, but at other parts of the circuit there is no distinguishable boundary-line. The intima is thickened, but not so much as the muscularis. The lining is beaded with enthothelial nuclei. *z* is an area represented more highly magnified by *D*.

FIG. 35.—DISEASED VEIN. (× 56.)

Another section of the vein shown by Fig. 34. There is great thickening of the wall, but it is of a different character. The opening is almost filled by irregular projections from the intima. One of these (*o*) is curiously folded and knotted. There is another somewhat similar knot of smaller size, and several irregularly shaped projections of the intima, which fill a large portion of the lumen. The muscularis is irregularly thickened. Parts of it are hard to recognize as involuntary muscle, being more like morbid fibroid tissue. *p* is distinctly muscular tissue. *m* shows the muscularis and intima shading together without a distinguishable line of separation. *n* marks a spot where the separation of the two coats is distinct.

C (× 220).—A portion of the muscularis from Fig. 34 more highly magnified. It shows the character of the long and narrow nuclei of the involuntary muscle.

D (× 220).—The region *z* from Fig. 34 more highly magnified. The central portion is morbid fibroid tissue, showing a fine mesh and containing a single connective-tissue nucleus. Outside of this is muscular tissue containing elongated muscular nuclei. It shows the manner in which the muscular tissue is torn apart by the growth of morbid fibrous tissue.

Fig. 34

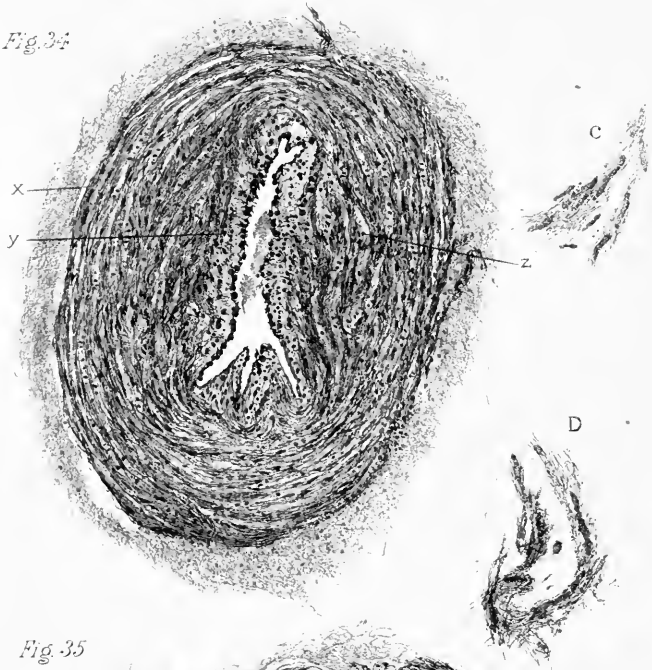
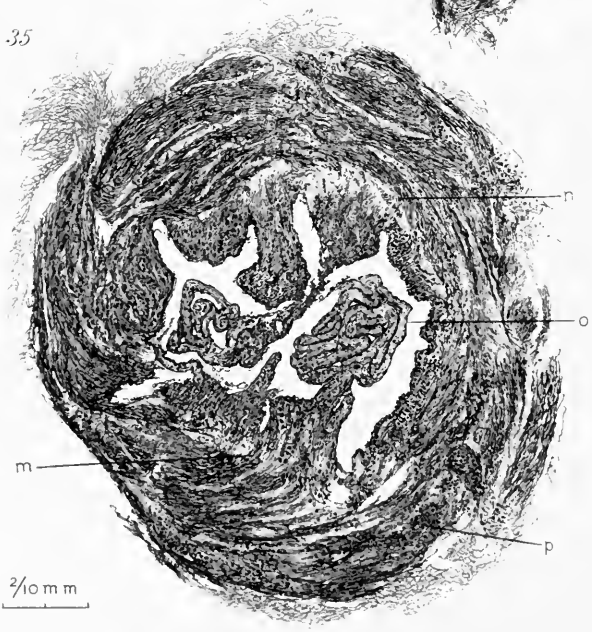


Fig. 35



was made through the skin, and a small piece of the thickened vein was removed from the right foot. In the removal blue venous blood was seen in the vessel, proving that it was a vein. When the cut end of the vein was examined with a hand lens, it was seen to be almost solid ; there remained only a very small opening.

"The illustrations are etchings which were made with the camera lucida ; the images of the objects under the microscope were reflected directly upon the steel plate, and drawn with the needle. They are, therefore, as nearly as possible, correct in dimension and detail. The pictures are two sections of the vein from the right foot, and the parts represented were separated by less than a quarter of an inch. Both views show the vessel to be almost closed. The vein appears as a nearly solid cord, instead of being a thin-walled tube, as natural veins are. The material filling the calibre is represented in the two pictures as being very different. In Fig. 34 there is a good deal of thickening of the intima, but much the greater part of the thickened tissue is the muscular coat, outside of which is the adventitia, which presents no evidence of disease. The intima is composed of fibrous tissue, in which the nuclei are easily distinguished, and the small slit-shaped opening is lined by a fringe of endothelial nuclei. Such an appearance of the intima and of the calibre is common in diseased arteries. The muscularis, on the other hand, which occupies quite two-thirds of the entire thickness of the vessel wall, is unlike anything that I have previously seen in diseased blood-vessels. Although it is correct to call it the muscular coat, by no means all of it is muscular tissue. The muscle fibres, with their long, narrow nuclei, are well represented in the drawing ; but it is also seen that the bands have been separated and thrown into wavy lines by a material which has grown in the midst of the muscular tissue, and has distorted it. This tissue is represented by the lighter colored areas in the picture, and they also contain many nuclei, but these are different in appearance from the muscular nuclei. Evidently a morbid fibroid tissue has grown in the muscularis, and at its expense. The appearances here represented are a more graphic demonstration than anything I have previously met that it is an error to call this increase of thickness of the muscular coat a hypertrophy, as is commonly said of it when it occurs in arteries, and that it is unreasonable to believe it can add to the power of useful contractility of vessels. Fig. 35 is very different

from Fig. 34, but a careful examination of it reveals that the disease which distorted the two parts of the vein had worked in a somewhat similar manner in both parts. The most striking characteristic is the large knots of twisted tissue which fill up a great part of the calibre of the vein. These masses resemble the knots that are formed by a large number of earthworms together, and they are the result of a growth of the intima which was so rapid as to outstrip the growth of other parts of the vein, so that the calibre could contain them only when coiled and twisted.

"There are parts of the calibre where the intima is moderately thickened and the endothelial cells are distinct in places, but they are generally somewhat enlarged and more rounded than is natural, and few, if any, of them appear as flat plates upon the inner side of the vessel. There is great thickening of the muscular coat, but this is less in degree than that represented by Fig. 34; and in places the muscularis and intima run together in such a way that it is impossible to say where the one ends and the other begins. The disease has gone so far that the muscular tissue bears little resemblance to natural muscle, and the intima as little to the natural intima of veins. Disease often totally changes the appearance of tissues, and this reminds one that at early embryological stages the various organs are so much alike that they can be recognized with the microscope only by their situations, and not by the arrangement or appearance of their cells. It seems as if disease is sometimes of the nature of a retrogression. The diseased tissues lose their natural characteristics, and fall back toward the lack of differentiation which is natural in the tissues of early embryos. The cause which seems to have the greatest influence in bringing about this retrogression is the growth of morbid fibroid tissue. In the forms of disease represented by the two pictures, the most striking feature in both is the growth of morbid fibroid tissue in the intima and in the muscularis.

"The disease that has been described, and which is shown by the pictures, would be attributed by most persons to syphilis, as the patient said he had been infected, and this explanation would generally be considered to be satisfactory and conclusive. It may be that the disease was syphilis, and there is no other cause at hand which better explains the disease of the vein, the extensive endarteritis, and the disease of the heart which the physical examination of the patient demonstrated. There is good reason for believing that

syphilis produces such vascular disease, but it would be a mistake to suppose that syphilis only can cause it." I know that syphilis is not always the cause of the disease, for I have seen it in patients who were not syphilitic but who died from other causes. For example, Fig. 36 is one of the radial veins of a negro woman twenty-seven years old, who died of typhoid fever. The disease is similar to that shown by both Figs. 34 and 35, for in addition to the exuberant growth of the intima, making it resemble earthworms, the muscularis is very much thickened and its tissue is torn apart and destroyed by the fibrous tissue which has grown among the muscular fibres. Fig. 37 is a section of the same vein as Fig. 36, and the section is from a portion of the vein very near that shown by Fig. 36. The character of disease, however, is quite different. The calibre is small but not nearly obliterated, and the wall is thick. A great part of the wall is formed of the muscularis, which is fibroid and has its muscular fibres torn apart so that it presents an open-meshed appearance. These two sections (Figs. 36 and 37) demonstrate in a striking way how the character of disease of blood-vessels varies at different parts of the same vessel and even of parts lying very close together. Another example of a vein with its calibre obstructed by proliferation of the intima is afforded by Fig. 49, which will presently be described. It was taken from a boy who died of meningitis and who certainly was not syphilitic.

It is not uncommon to find the muscular coat of the radial veins thickened and the fibres separated by the growth of morbid fibroid tissue in persons whose radial vessels had been felt during life to be thickened. In my book on the "Origin of Disease" [1] there is a picture of a portion of the vena cava of a man fifty-seven years old, who died of Bright's disease, which shows thickening of the muscular wall and separation of its fibres. As it has now been shown that these changes of the veins occur in persons suffering with other diseases, and who were not syphilitic, it would be an error to emphasize too much the fact that the patient from whom the vein represented by Figs. 34 and 35 was taken had been infected with syphilis. It is now well known that the form of endarteritis which used to be considered syphilitic arises also from a variety of other causes, and the appearances of the veins from which the illustrations were made

[1] The Origin of Disease, by Arthur V. Meigs, page 59 and Fig. 36.

demonstrate that endophlebitis is due to other causes besides syphilis. It is singular how a part of a vein may be excessively diseased and another portion very near may be quite differently diseased ; this has been shown by Figs. 36 and 37. Fig. 38 presents a condition in some respects parallel but in others very different. It shows the same superficial vein of the skin of the foot as Figs. 34 and 35, but the section was so cut as to include one of the branches that ran along the sides of the toes. The main vein presents the same character of disease as that shown by Fig. 34, and which has already been described, but the branch offers a striking contrast. It is thin-walled and does not appear to be diseased, and, what is perhaps more striking still, structurally it is not a vein at all, but is a capillary. The transition from the vein, with walls so thick that its calibre is almost obliterated, to the thin-walled capillary which seems to be normal, is quite sudden. It seems as if nature had broken her rule, which is, that, almost without exception, she draws no hard lines and does nothing abruptly. The question suggests itself—and it is one of interest—whether it can be that many of the small superficial cutaneous veins which are easily seen with the unaided eye may be really capillaries and not veins at all. The veins at the sides of the toes are often easy to see, and they are filled with blue blood like other veins, but the vessel (*c*, Fig. 38) shown by the illustration has not three coats and it is composed of endothelium alone.

Figs. 39, 40, and 41 are three arteries with their accompanying veins. The arteries, although quite unlike the accepted standards of the normal, show nothing unusual ; but the veins are diseased, and they are in some respects affected alike and in others differently. All of them are thick-walled, but the nature of the tissue composing the walls is different. They are from persons of very different ages and who died of different and unrelated diseases. Fig. 39 is from the mesentery of a negro infant one year old that died, after an illness lasting six months, of chronic catarrhal pneumonia following whooping-cough. The artery is thick-walled, but presents no other point of interest. The vein also has thick walls, and it shows fibroid disease of the muscularis of the same character as that shown by Fig. 34 and the other veins described in connection with it. Fig. 40 shows an artery and a vein from a negro woman twenty-seven years old, who died of tubercular meningitis and pulmonary tuberculosis and ulcer

FIG. 36.—FIBROID VEIN. (× 50.)

From the same case as Figs. 29, 37, and 42. A radial vein. The wall of the vein is greatly thickened. A great part of the thickening is of the muscular coat, which is of loose texture, like other diseased veins that are represented by the illustrations. Morbid fibroid tissue was deposited in the muscularis. The lumen is almost filled by threads like earth-worms, which are attached to the lining of the vein. It is as if the intima had grown very voluminous and then been cast loose from its attachment. Fig. 37 depicts a section cut from the same vein and close to the part shown by Fig. 36. The muscularis is similarly diseased in both sections, but there are no loose shreds in the lumen in Fig. 37.

FIG. 37.—FIBROID VEIN. (× 50.)

From the same case as Figs. 29, 36, and 42. A section of the same vein that is represented by Fig. 36 and cut close by the other section. It exhibits similar thickening of the wall and the same diseased loose-textured state of the muscular tissue, but there are no loose shreds from the lining hanging in the lumen.

FIG. 36.

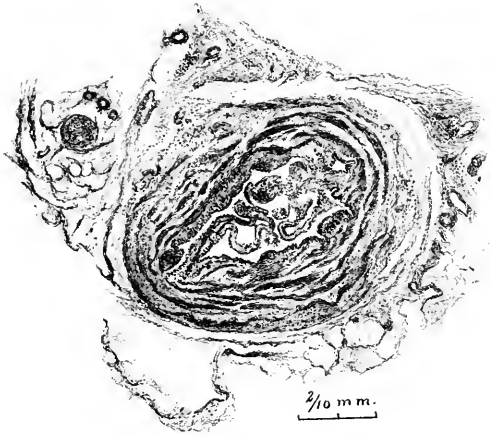


FIG. 37.

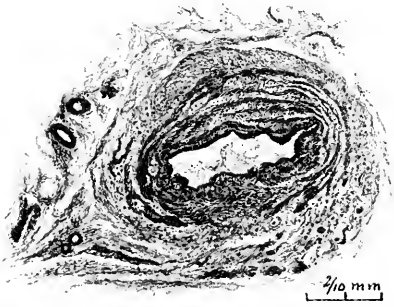
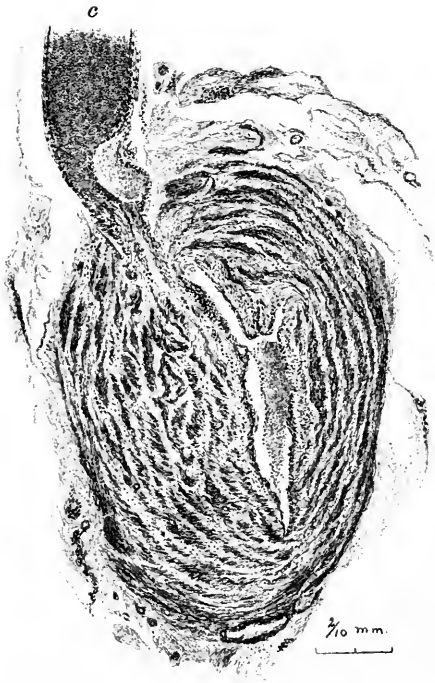


FIG. 38.—DISEASED VEIN WITH CAPILLARY BRANCH. (× 50.)

From the same case as Figs. 34 and 35. The same vein, with a portion of one of its branches (*c*) that ran at the sides of the toes. The vein shows the same disease of the three coats as Fig. 34. The branch, however, which was large enough to be easily seen with the naked eye before it was removed from the foot, presents the appearances of a capillary. The most striking characteristic is the sudden transition from disease to the normal. The vein is thick, so that its lumen is almost closed, and this was perceived during life, while the branch is thin and seems quite normal.

FIG. 38.



of the stomach. The artery and vein are from a portion of the stomach close to the ulcer. The artery might almost be regarded as a type of the normal of blood-vessels of its size. The vein is thick-walled from fibroid overgrowth of precisely similar character to that represented by Fig. 31. The fibroid disease shown by Figs. 31 and 34 and by Figs. 39 and 40 is of the same general character, for in all four of them the principal lesion that can be recognized is the excessive growth of fibroid tissue in places where under natural conditions there is very little of it. As seen in Figs. 31 and 40 the muscular tissue is so torn apart, and there are so many openings through the muscular layers to the adventitia outside, as to suggest that the fibroid disease had its origin in the adventitia, or entirely outside the vessels in the perivascular connective tissue, and that the fibrous tissue forced its way into them just as growing cancer penetrates adjacent tissues. This parallel was suggested and is discussed at page 51. The fact that exactly the same sort of lesions may be found to result in the veins of persons dying of such different diseases as tuberculosis and chronic pulmonary inflammation, and at such different ages as twenty-five years and one year, is both striking and curious.

Fig. 41 is a drawing of an artery and a vein of the colon of a woman twenty-six years old who died of typhoid fever. The artery is thick-walled, but it presents no points of special interest nor anything worthy of discussion here. It was included merely to set off the vein and to give a more graphic and complete representation. The vein is even thicker-walled than the artery, and the tissue composing the wall is of a very different character from that of the veins shown by Figs. 39 and 40. The tissue does not look like involuntary muscle, of which the greater part of the walls of the veins depicted in Figs. 39 and 40 is formed. If there is any muscular tissue in the wall of Fig. 41 it has been so much changed by disease that it is no longer recognizable. There are very few fibres extending circularly around the vein, as there are in Figs. 39 and 40, and none of the long, narrow nuclei which are ordinarily the most prominent characteristics of the muscularis of blood-vessels. On the contrary, the nuclei are large and are nearly round. This state of disease of the vein—the thickening of the wall, the swollen and rounded character of the nuclei, and the absence of the circular fibres—is to be attributed to the acute

inflammatory disease of which the patient died. Typhoid fever lasts but a few weeks, and it is probable that up to the time of the onset of the fatal attack the blood-vessels of the patient were normal. The appearance of the vein Fig. 41 stands in marked contrast to that of the veins Figs. 39 and 40, which were taken, as has already been said, from patients who died of chronic diseases.

Fig. 42 represents a blood-vessel of a negro woman twenty-seven years old who died of typhoid fever. The drawing was made from a section of the radial artery, its accompanying blood-vessels, and surrounding tissue. From its situation and appearance I believe the vessel to be a minute vein, but it is so entirely unlike any normal blood-vessel that it is impossible to be certain that it is not an arteriole or a capillary. Its cell structure is more like epithelium than like any of the other human tissues, and there is nothing that in the least resembles the intima, the muscularis, or the adventitia of normal blood-vessels. In my book on "The Origin of Disease,"[1] I described a blood-vessel which in many respects resembles Fig. 42. That vessel is from the thickened mucosa of the colon of a man who died of acute dysentery, and I took it to be an arteriole; but, as in the case of Fig. 42, it is impossible to be sure whether the vessel is an artery, a vein, or a capillary. They are both entirely unlike normal blood-vessels, and the tissue that composes them is more like epithelium than like any other normal tissue. It is strange how disease can change the normal tissues so much as to render them unrecognizable. What produces such a condition as this I am entirely unable to say, and it would be quite useless to indulge in conjecture when there are no facts upon which to base an opinion.

My description of disease of the veins is imperfect. It was not my purpose, however, to write a complete account of all that is known of the subject, but to describe what I have myself seen. It has been impossible to classify disease of the veins in a satisfactory manner, for there is not enough known of the subject even for the foundation of a classification.

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[1] Page 50 and Fig. 16.

FIG. 39.—THICKENED ARTERY AND DISEASED VEIN OF THE MESENTERY. (× 105.)

From a negro infant one year old that died of chronic catarrhal pneumonia. The lower flattened vessel is an artery, of which the muscular coat is somewhat thick,—a very common change in chronic disease. The vein, which is above, is very thick-walled, and the nature of the tissue is similar to that shown by Fig. 34.

FIG. 40.—ARTERY AND DISEASED VEIN FROM STOMACH. (× 50.)

From a negro woman twenty-five years old who died of tubercular meningitis and pulmonary tuberculosis and ulcer of the stomach. The vessels lie close to the ulcer. The artery, which is above, is of normal appearance. The vein, which is below, has greatly thickened walls. The tissue is of the same nature as that shown by Fig. 34. There is muscular tissue which is torn apart by fibrocellular material which has grown in it, and the intima is more thickened than is usual in veins.

FIG. 41.—ARTERY AND DISEASED VEIN OF THE COLON. (× 105.)

From a woman twenty-six years old who died of typhoid fever. The vessel above is the artery and that below the vein. The artery is perhaps a little thickened. The vein is much diseased, being thick-walled and composed of tissue quite unlike that of normal veins. This tissue is somewhat like that shown by Fig. 34, but the nuclei are round or rounded. It does not look like muscular tissue.

FIG. 39.

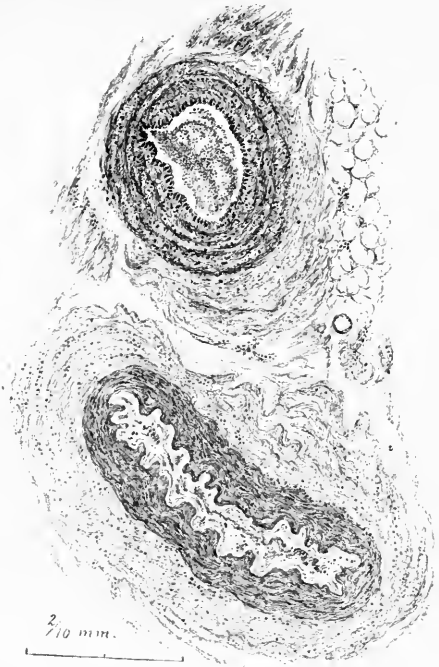


FIG. 40.

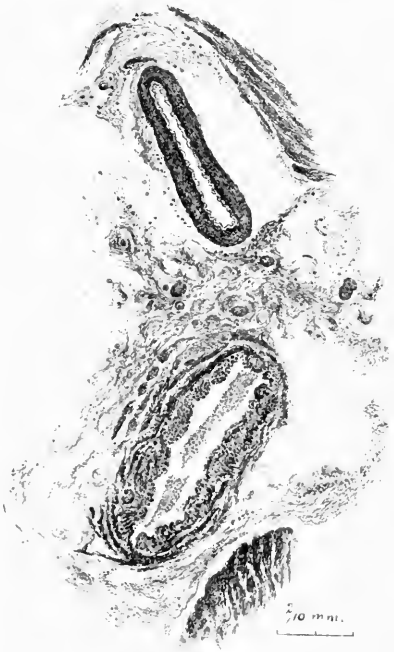


FIG. 41.

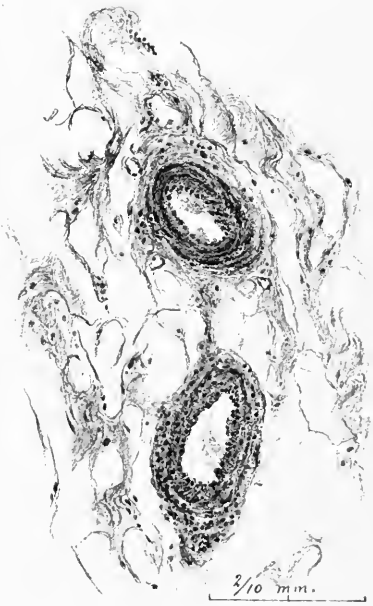


FIG. 42.—BLOOD-VESSEL OF ATYPICAL UNUSUAL STRUCTURE. (× 240.)

From a negro woman twenty-seven years old who died of typhoid fever. A blood-vessel lying near the right radial artery. Figs. 29, 36, and 37 are from the same patient. There is a strong general resemblance to a tiled pavement. The tissue is more like epithelium than like that of ordinary arteries, veins, or capillaries, and it is impossible to know to which class it belongs.

FIG. 42.

CHAPTER VI

Disease of the Radial Arteries and Veins

Disease of the radial artery is often recognized during life because the custom of feeling the pulse at the wrist directs the attention of physicians to its condition more than to that of any other blood-vessel. The radial artery can frequently be felt to be thickened, and be seen to pulsate. Any great thickening of it is always morbid, and constant excessive visible pulsation indicates the existence of disease of the heart, or of the vessel itself, or of both. Evidence of disease obtained by feeling the pulse has heretofore usually been thought to denote disease of the heart unless it was considered that the artery itself was diseased, and very little attention has been paid to the state of the veins. My own experience has shown me that disease attacks the veins about as frequently as the arteries, and that it is very common for them both to be affected. There is even less known of the effects of disease of the veins than of those of the arteries, and almost nothing is known of clinical symptoms which may result directly from disease of the veins or arteries. Disease of the radial blood-vessels found in feeling the pulse is generally due to fibroid degeneration, which is the curious process that I have said is inevitable to the advance of years and is not rare in the young. When disease of the radial artery has been recognized during life, it is often possible to be almost certain that disease of other blood-vessels also exists. The exact effects of these physical changes of the blood-vessels are as yet unknown. It is, however, well known—and the fact should be kept constantly in mind by physicians—that extensive disease of the blood-vessels may exist, especially in old people, and yet good general health be maintained for long periods.

Fig. 43 shows the right radial artery and veins from a negro man nineteen years old who died of typhoid fever. Fig. 44 represents the left radial artery and one vein from the same patient. Generally there are two veins accompanying the radial artery, and probably the reason why only one is to be seen in Fig. 44 is that the second was overlooked and left behind when the piece of tissue was dissected from the wrist. The contrast presented by these two sets of radial

arteries and veins is very striking. The vessels depicted by Fig. 44 may be taken as almost typically normal, and if they are compared with those of Fig. 13, which I have described as normal, it will be seen that the two sets of vessels are very nearly alike. . The muscularis of the artery (Fig. 44) is of irregular thickness at different parts of its circumference, and it is probably a little thicker than normal. I do not think the intima can be said to be diseased, for it is not usual to find it any thinner in the radial artery. The vein is very similar in appearance to the one shown by Fig. 13. The accepted standard of the normal appearance of veins seems certainly to be incorrect as far as concerns the radial vein at least. The common conception of veins is that they are a good deal like the arteries, being composed of three tunics, and that the tissue forming these three tunics is of similar nature to that of arteries. It is supposed that the differences of the two kinds of vessels one from another are that the tunics are of different degrees of thickness and that the amount of elastic tissue is different. Veins such as are shown by Figs. 44 and 13 differ from arteries much more widely than ordinary descriptions and the illustrations in most text-books represent. Fig. 43 presents a very different state of things from Fig. 44. The artery is thick-walled and the thickening is irregular in its distribution. The intima cannot be said to be abnormal; it has very much the same character as that of the artery in Fig. 44. The adventitia also appears to be normal, but the muscularis is the diseased tunic. The irregularity of thickness of the vessel at different parts is confined entirely to the muscularis, which by measurement is twice as thick to the right as it is to the left in the drawing. If the vessel be studied with greater amplification than was used to make the illustration, it is seen that the tissue is diseased. There is not simply an increase of the muscular tissue, constituting a hypertrophy which might have endowed the vessel with an added power to perform its function, but it is seen that there is hyperplasia which is due to degeneration. The veins shown by Fig. 43 are also very different from the one shown by Fig. 44. The muscular tissue which composes the greatest part of the walls of the veins in Fig. 43 is loose meshed, like that shown by Fig. 34 and in the vein directly above and to the right of the artery, and in this vein the intima is proliferated and hangs loose in the lumen in the same way as that shown by Fig. 35. The extent of this peculiar disease is not great in

FIG. 43.—DISEASED RADIAL ARTERY AND VEINS. (× 20.)

The right radial artery and veins from a negro man of nineteen years who died of typhoid fever. The artery is thick-walled, the thickening being nearly twice as great upon one side as on the other. Both the intima and the muscularis are thicker than is generally represented as natural. The veins are not natural, being slightly thick-walled, and the muscular tissue presents to a slight extent the loose-meshed appearance that is common in diseased veins. There are shreds which hang from the lining lying in the lumen of the small vein above and to the right of the artery. These diseased vessels present a strong contrast to the left radial artery and vein of the same patient, which are represented by Fig. 44.

FIG. 44.—NEARLY NORMAL RADIAL ARTERY AND VEIN. (× 20.)

The left radial artery and vein from the same man as the vessels represented by Fig. 43. The artery is to the right and the vein to the left. The two blood-vessels are but slightly abnormal, as may be recognized by comparing them with Fig. 13. The contrast with Fig. 43 is very striking.

FIG. 43.

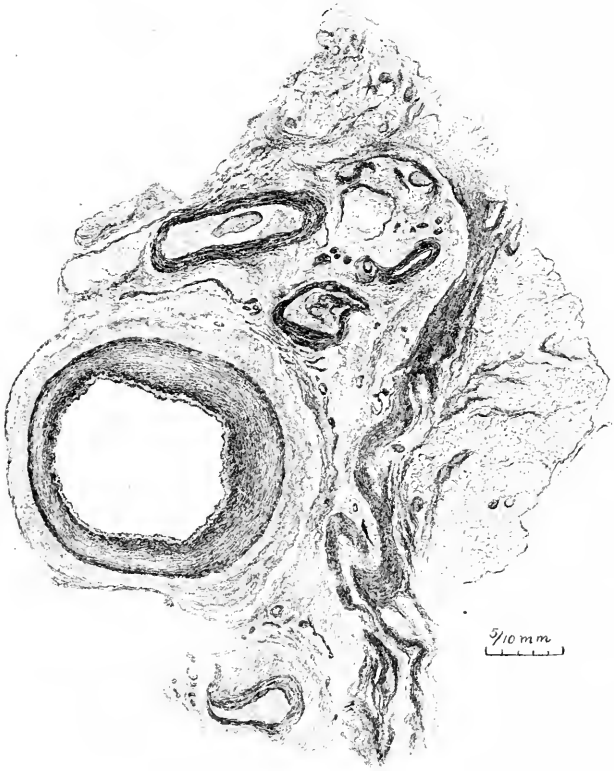
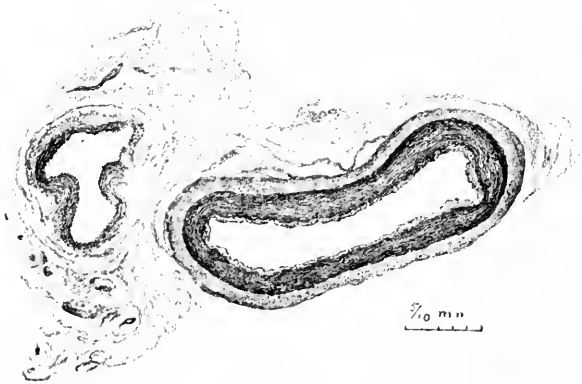


FIG. 44.



the present case, for the calibre of the vein is not nearly filled and it contains quite a mass of red blood-corpuscles ; but if the vessel is examined with greater amplification the disease can be seen to be of exactly the same character as that shown by Fig. 35, though it has not progressed so far. The most striking feature, however, of Figs. 43 and 44, which, as has been said, are the right and left radial arteries and veins from the same patient, is that the one set of blood-vessels is so much diseased and the other is practically normal. It is impossible to comprehend why two sets of blood-vessels that were probably exposed to the same influences to cause disease of them or to leave them healthy should be so totally different.

Another interesting point is the discovery, in a young man of nineteen years who died of typhoid fever (which is an acute disease that runs its course in a few weeks), of such a diseased artery as that shown by Fig. 43. The thickening of the muscularis, which I believe to have been the result of morbid fibrosis, was probably of slow growth and very likely it existed for a good while before the acute fatal attack. If such was the case the patient suffered with chronic latent disease which gradually undermined his health for some time before the outbreak of the acute attack which ended fatally. Fibroid disease of the blood-vessels, which is usually regarded rather as a disease of persons of advanced years, is striking when it occurs at nineteen years of age. In my book on the "Origin of Disease" I have discussed this curious latency of chronic fibrosis, and have shown that a careful examination of the bodies of those dead of acute disease often reveals the presence of lesions of chronic nature which must have long antedated the acute fatal attack, and may very probably have played an important part in rendering the individual liable to the acute disease.

Figs. 45 and 46 represent two sections of the same radial artery and veins of a negro man twenty-four years old who died of tuberculosis. The sections are of parts of the vessels that were not more than a quarter of an inch apart. It is strange that two portions of the same vessels separated by such a slight distance should be so different. As shown by Fig. 46, the artery is nearly round and its wall is a good deal thicker than in Fig. 45, which is of irregular shape. Part of this difference may be due to greater shrinkage of the artery shown by Fig. 46 ; but, as the two pieces of tissue from which the sections were

cut were subjected to the action of the same reagents, it is unlikely that the difference is wholly due to the mode of preparation ; it is much more probable that it is the result of disease. Besides, it was ascertained during the life of the patient, by feeling the pulse at the wrist, that the radial vessels were thickened. The muscularis of the arteries is thick in both of the sections, and the cause of this thickness is degeneration, not hypertrophy. The intima also is unnaturally thick, as may be recognized by comparing it with Fig. 13, which is normal. The veins are even more evidently diseased than the arteries. It is impossible to be sure that all the vessels surrounding these two sections of the radial artery are veins, although some of them can be recognized with certainty. The two minute vessels, *a* and *c*, Fig. 45, are entirely closed by plugs of tissue. They are probably veins, but they are so much changed by disease that it cannot be said that they may not be arterioles. Examination of these two blood-vessels with greater amplification demonstrates that the plugs in the calibres are not mere blood-clots, but are formed of well-organized fibrous tissue. It is not rare for blood-vessels to become thus occluded, and the tissue that grows in the lumen may be well organized and may contain a vascular supply of its own. Such a vessel is shown and described in my book on the "Origin of Disease" (page 45 and Fig. 13). Two of the veins, *b* and *d*, Fig. 45, are thick-walled, and the tissue forming the walls is almost entirely muscular. This muscular tissue is loose meshed and torn apart by the growth of fibrous tissue between the threads of muscle, and in one of the veins there is slight proliferation of the intima and a loose shred hangs in the lumen. The disease is evidently an early stage of the same process that is shown by Figs. 34 and 35. The veins in Fig. 46 are even more extensively diseased than those in Fig. 45, all of them being thick-walled and the walls formed almost entirely of muscular tissue which is open meshed, owing to fibroid disease. One of the veins (*e*) is nearly closed. There are loose strands of the overgrown intima hanging in the lumen and a fan-shaped mass which seems to be composed of muscular tissue which has undergone fibroid degeneration. This obstruction of the veins is a very curious form of disease, and it is evident that it is not uncommon.

Figs. 47, 48, 49, and 50 show the radial artery and veins of a boy fifteen years old who died of acute meningitis. It was perceived

FIG. 45.—THICKENED RADIAL ARTERY AND DISEASED VEINS. (× 20.)

From a negro man twenty-four years old who died of tuberculosis. The artery is the large vessel in the centre. Its three coats and the plicated membrane are easily distinguished. The intima and muscularis are thicker than natural, and the plicated membrane more folded than usual. *a*, a vein entirely closed by a plug of organized tissue. *b*, a vein with thick and diseased walls (of somewhat the same nature as Fig. 34) and strings from the lining hanging in the lumen. *c*, a small vein in which, when more highly magnified, the plicated membrane can be seen, and with the lumen entirely closed by an organized plug of tissue. The vein is a solid rod. *d*, a vein with thickened walls composed of loose-meshed, diseased muscle. None of these veins have walls in the least like natural walls of veins.

FIG. 45.

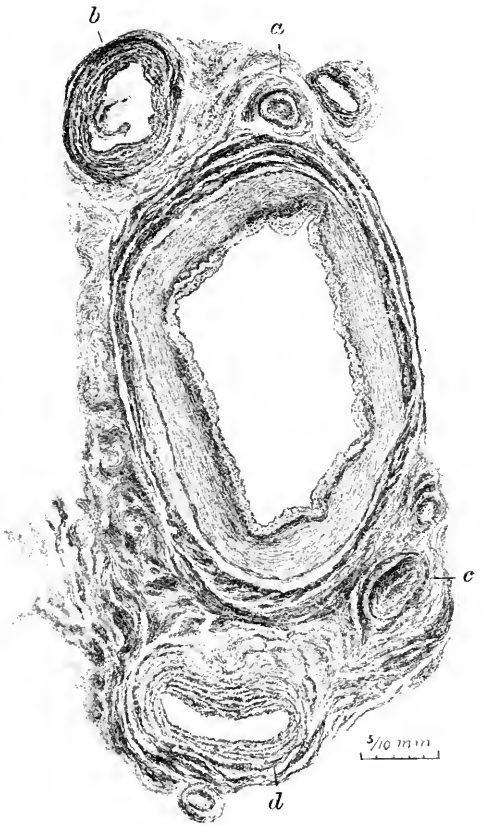


FIG. 46.—THICKENED RADIAL ARTERY AND DISEASED VEINS. (× 20.)

The same artery and its surrounding veins as are shown by Fig. 45. The general characteristics are very similar. The walls of the artery are thicker, the plicated membrane is even more folded, and the calibre is smaller. It may be more shrunken than the other section, although they were cut less than a quarter of an inch apart. *e*, a vein with thick walls and with twisted strands of tissue from the lining resembling a fan in the lumen. *f* and *g* are veins with thickened walls which are composed entirely of loose-meshed, diseased muscular tissue.

FIG. 46.

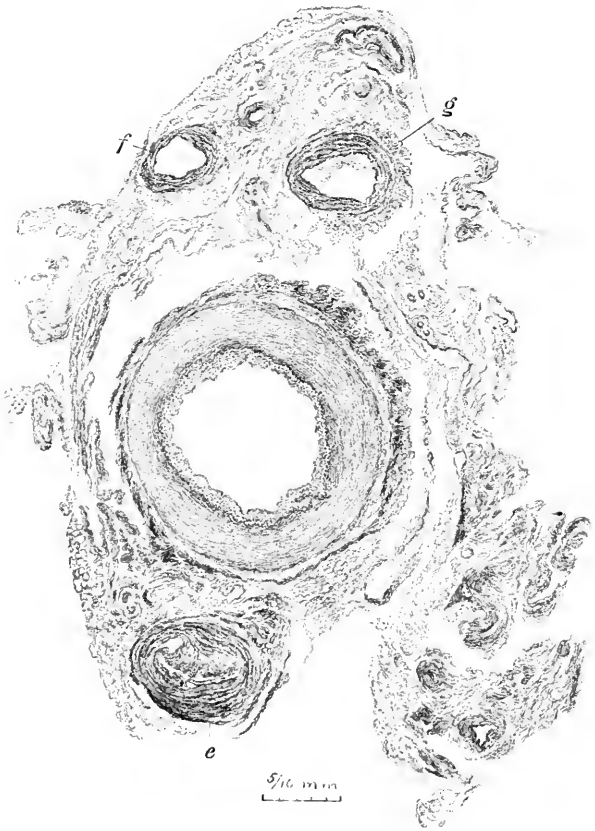
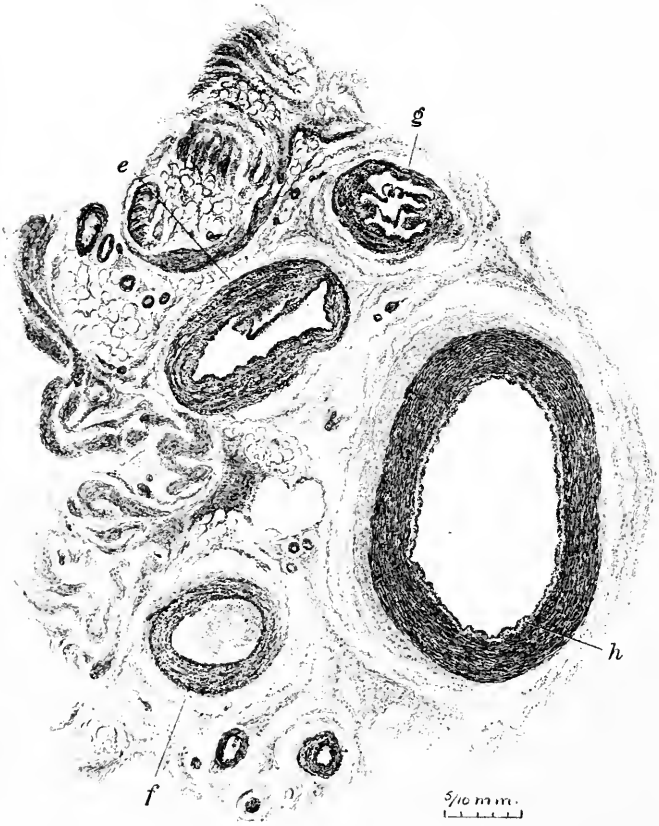


FIG. 47.—DISEASED RADIAL ARTERY AND VEINS. (× 20.)

From a boy fifteen years old who died of acute meningitis. The artery, which is the largest vessel, is thick-walled, the muscularis especially being thick. *h* is a region represented more highly magnified by Fig. 48. *e*, *f*, and *g* are veins and they are all diseased. Their walls are formed of tissue like that of the muscularis of Fig. 34. *e* is thick-walled and is very like *f*, except that there is a large band hanging loose in the lumen. *f* is thick-walled and Fig. 50 is an enlarged view of another section of the same vein. *g* is a thick-walled vein with bands hanging across its lumen. Fig. 49 is an enlarged view of the vein *g*.

FIG. 47.



during the life of the patient, when the pulse was felt at the wrist, that the vessel or vessels were stiff. Such stiffening as this, which is ascertained to be present by feeling the pulse, is commonly considered to denote that the radial artery is thickened owing to atheroma or to calcification of its walls or to some other disease. My own experience has proved to me that under such circumstances the veins often participate in the disease, and a glance at the drawings at once shows that all of the veins as well as the artery are diseased. Thickening of the walls of the blood-vessels, which it is well known occurs almost inevitably in old people, is very curious, but there is almost nothing known of its cause except that fibrosis is a part of the process. This, however, does not touch the real question of the cause. That similar thickening of the blood-vessel walls should occur also in young people (the vessels seen in Fig. 47 were taken from the body of a boy of fifteen years) is even stranger and still more beyond our power to explain. In my book on the "Origin of Disease" I have discussed the question of this strange condition, which is like age in youth, and in that book, as well as in this one, there are included a number of drawings of blood-vessels from the bodies of young persons which show the thickening of their walls that is generally believed to be characteristic of age. The boy from whom the blood-vessels (Fig. 47) were obtained died of acute meningitis and he was ill for many weeks. During the course of the illness he became emaciated to the last degree and, as commonly occurs under the circumstances, he assumed more and more the appearance and expression of age. The tissues were dry and shrivelled, and the face especially resembled that of an old man, the skin being wrinkled and tightly drawn over the bones, which stood out, and the head looked almost like a dried skull. It is pitiable to see a boy, and perhaps even more so to see an infant dying of wasting disease, assume the expression of old age. Examination of the body under such circumstances invariably reveals the existence of some of the lesions of age, and among them of thickening of the blood-vessels.

It is easy to see that the artery pictured in Fig. 47 is diseased, for its wall is thick, and Fig. 48, which is an illustration of a portion of it more highly magnified, shows other abnormal conditions. The intima probably is a little thicker than is normal, and the plicated membrane exhibits a curious condition which quite commonly

exists in arteries under such circumstances and which must be owing to disease. In some places it is distinctly visible, and in others it cannot be seen. Its disappearance must be due to its having become cellular and blended with the intima and muscularis. The normal plicated membrane is acellular and clear like the cornea of the eye, but under the influence of disease, especially of inflammation, it becomes cellular and opaque. To the left in Fig. 48 the plicated membrane is easily distinguishable, but to the right it cannot be seen. This form of disease I have described in my book on the "Origin of Disease" (page 43, Fig. 8), and I have shown that it may occur even in infancy.

Fig. 48, which depicts a portion of the artery more highly magnified, shows better than Fig. 47 that the muscularis is diseased. It is thicker and less rich in nuclei than is natural in involuntary muscular tissue. This I believe to be due to the growth of morbid fibroid tissue in the muscularis. The effect of the post-mortem shrinkage is strikingly shown by the situation of the muscular nuclei, which are irregularly placed, instead of having their greatest length running in the direction of the circumference of the vessel, as is seen in Fig. 11, which exhibits more nearly the conditions existing during life. Fig. 47 shows that all the veins included are diseased. The walls of all of them are thicker than normal, and two of them, *e* and *g*, have shreds or partitions which are partly, at least, formed of the intima hanging in their openings.

In Fig. 49 is seen the vein *g* of Fig. 47 more highly magnified. The disease is a combination of the morbid conditions shown by Figs. 34 and 35. There are two strings hanging across the calibre of the vein. Parts of these are light and are composed of material like the structureless endothelium of the intima, and there are endothelial nuclei in them. Near the points of attachment of the strings they are heavier and contain muscular tissue. The wall of the vein is thicker than is natural, and much the greatest part of it is composed of loose-meshed diseased involuntary muscle. The muscular tissue, instead of being composed almost entirely of threads and elongated nuclei running principally in the direction of the circumference of the vessel wall, as is natural, is formed of material which does not appear to have any orderly arrangement. There are scattered bits of muscle which run in various directions, and between these are por-

FIG. 49.—DISEASED RADIAL VEIN. (× 50.)

The vein *g* from Fig. 47 more highly magnified. There are two strings or partitions extending across the lumen of the vein. These look like thickened shreds of endothelium from the lining of the vein. There are also several irregular masses of tissue projecting into the lumen. The wall of the vein is of very varying thickness, and it is composed of muscular tissue and morbid fibroid tissue which has grown in it. The whole appearance is like another phase of the state of disease shown by Figs. 34 and 35.

Fig. 49.

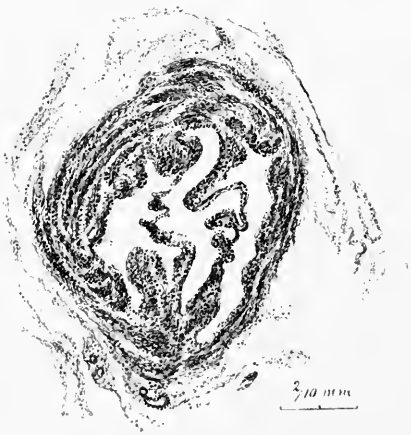


FIG. 49.—DISEASED RADIAL VEIN. (× 50.)

The vein *g* from Fig. 47 more highly magnified. There are two strings or partitions extending across the lumen of the vein. These look like thickened shreds of endothelium from the lining of the vein. There are also several irregular masses of tissue projecting

tions of fibrous tissue. This vessel, as much as any one that I have ever examined, seems to me to demonstrate that part of the cause of such disease is the irregular growth of fibrous tissue in places where under natural conditions there is very little of it. The contrast between such involuntary muscle as this and the muscularis of a normal vein is most striking. Altogether this vein is a curious one and the disease is very interesting.

Fig. 50 is an enlarged view of the vein *f*, Fig. 47. The character of the disease is very similar to that shown by Fig. 34. The calibre of the vein is small and it contains blood-corpuscles. The wall, which is greatly thickened, is composed principally of diseased muscular tissue, and the drawing shows that the fibres and the nuclei of the muscle have been torn apart by fibrous tissue which has insinuated itself between them. In this vein, as well as in Figs. 34 and 31, the morbid fibrous tissue can with certainty be recognized as such. In some of the drawings it is possible to see that the muscular tissue is torn apart, but the nature of the material lying between its fibres cannot be definitely identified. This may be because of imperfect preservation of the tissue, or owing to poor staining, or there may be some other reason why the spaces between the shreds of muscle look as if they were empty. The intima shown in Fig. 50 is thicker than that of any of the other veins of which drawings are included. There is no law that I have been able to discover governing the relative amount of thickening of the intima and muscularis of arteries and veins that takes place as a result of disease. Most of the thickened veins that I have studied have exhibited disease and increase of the muscularis, but the condition of the intima has varied. In none of them has the intima been thickened to anything like the degree that it is common to see in arteries. Fig. 50 shows greater thickening of the intima than any other vein that I can remember to have seen. On the other hand, it is quite certain that in arteries with thick walls, it is the intima that is diseased and thickened in the great majority of cases. The radial is more liable to undergo thickening of the muscularis than any other artery that I have examined, but, in addition, as has been shown in this chapter, there is apt to be more or less disease of the intima as well. The kind of thickening and disease of the intima that is common in the arteries of the heart and kidney, the nature of which will be shown in the chapters upon those two

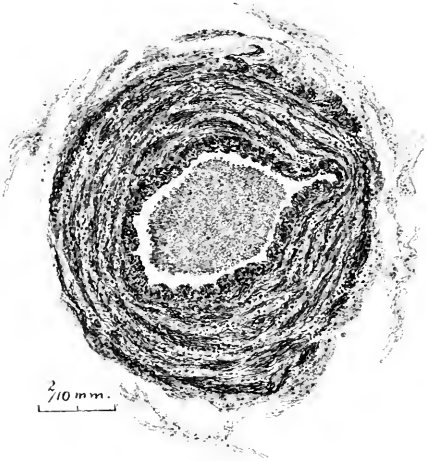
organs, I have never seen in a vein, and it certainly cannot be as common in the veins as it is in the arteries. There must be some reason why arteries are so much more liable to disease of their lining membrane than veins, but, as has been said, almost nothing is yet known of the law which governs the relative degrees of thickening of the two tunics that occur. Even less is known of disease of the adventitia; but I have already discussed this subject in connection with the peculiarities of the blood-vessels shown by Fig. 33. The confusion which arises owing to the difficulty in distinguishing between adventitia and perivascular connective tissue is a subject that I have more than once mentioned, and it is one that has always to be contended with in studying the adventitia both of arteries and veins.

My discussion of the subject of disease of the radial arteries and veins is quite incomplete, but I think I have been able to add a little to what is known of it. The observation that the veins as well as the radial artery are thickened, when thickening is discovered by feeling the pulse at the wrist, is one of importance, and the nature of the lesions of the radial veins is very curious. The most striking of these is the proliferation of the intima, which produces in the calibre of the vein a mass that in section looks like a bunch of entangled earthworms. Veins so diseased are most curious objects to examine, but the cause of the disease is as yet unexplainable. More extended study of this disease of the veins which causes thickening of their walls and reduction of their openings, and therefore interference with their power to carry blood, may some day lead toward an explanation of that strange and widely prevalent disease — fibroid degeneration. There is no part of the body that is not liable to be affected by it, nor is there any period of life at which human beings are secure from its insidious invasion. It is an inevitable accompaniment of age, and it often attacks young infants. There is good reason to believe that it has its beginnings in or near the blood-vessels, but just where and how it begins has not yet been discovered. The normal and diseased veins which are shown by the drawings indicate that in structure they differ from arteries more decidedly than is generally supposed, and that the ordinary descriptions of veins need a good deal of revision.

FIG. 50.—DISEASED RADIAL VEIN. (× 50.)

Another section of the vein *f* from Fig. 47 more highly magnified. The wall is very thick, and it is composed in great part of muscular tissue into which a large amount of morbid fibroid tissue has grown. The intima also is thickened. The disease is similar to that shown by Fig. 34.

FIG. 50.



CHAPTER VII

The Blood-Vessels in Inflammation, in Tuberculosis, and in Syphilis

As a result of inflammation, of tuberculosis, and of syphilis the tissues undergo changes and the blood-vessels are often diseased. These lesions of the vascular system have been quite extensively studied, and it has been supposed that the different diseases could be recognized from a study of the pathological changes of the blood-vessels that they cause. My own investigations have made me believe this to be impossible. The mistake is made of studying the tissues of a man who has died of one of the diseases, and then, if lesions of the blood-vessels are found, of supposing that they are peculiar to the disease of which the patient died. No consideration is given to the facts that the vascular changes may be incidental and that similar lesions may arise from other causes. It is my opinion that there is no lesion of the blood-vessels which is peculiar to inflammation, to tuberculosis, or to syphilis, and this opinion is based upon the examination of a great many blood-vessels. The mistake of supposing that particular diseases can be recognized from the peculiarities of a few cells, or by the appearance of some minute lesion of a blood-vessel which can be seen only with the microscope, is much less common to-day than it was a few years ago. It is acknowledged, for instance, that tubercular disease cannot be recognized by the examination of any one field under the microscope, because much of the tubercular tissue is like other tissues, and even giant cells, which at one time were believed to be peculiar to the tubercular process, are now well known to be due to other causes and to be often found in non-tubercular tissues. Tuberculosis can only be recognized post mortem by the study of the disease in the gross together with a careful consideration of all the information to be derived from the fullest examination of all the tissues and in every known way. There is no cell, nor is there any grouping of cells, that is peculiar to tuberculosis. The same thing is true of inflammation and of syphilis. In studying the tissues of persons who have died

while suffering with the diseases under consideration, the points that have struck me most forcibly are the similarity of the lesions of the blood-vessels found in all three, and, on the other hand, the frequent entire absence of disease of the blood-vessels in cases of those diseases which are generally supposed most surely to produce it. My illustrations show the general similarity of the lesions.

Fig. 51 is an illustration of a portion of the wall of the inflamed and atheromatous aorta of a negro man fifty years old who died of endocarditis. The adventitia and a portion of the muscularis are included by the drawing. There are several areas which distinctly show inflammatory cellular exudation, but the most peculiar feature here observed is the condition of the blood-vessels. The largest one of these vasa vasorum, of which three large ones are included, is very thick-walled and is of unnatural appearance. There are other smaller vessels shown, but they are thin-walled and are like capillaries in structure. It is impossible to ascertain whether the three thick-walled vessels are new growths which resulted from the effects of the inflammation or are only natural blood-vessels changed and thickened by disease which existed when the patient was in apparent health. My own inclination is to believe that they are new vessels which failed to attain a natural development. The middle one of the three is almost a solid cord, for there is only a very minute channel in it and that is not centrally placed. The tissue of which it is composed is unlike any that exists in natural blood-vessels. The two others also are totally unlike normal vessels. The manner in which a bit of the adventitia is dragged into an arch over one of these vessels produces an odd effect. The distortion must be the result of increase in size of the vessel which was at one time smaller. As it grew it pushed the adjacent tissue to one side and caused the formation of the arch. The subject of the growth of new blood-vessels is discussed in Chapter III. It is curious to find such vessels in the wall of the inflamed and thickened aorta of a man who died of endocarditis.

Fig. 52 represents an arteriole and a venule of the ileum of a woman twenty-six years old who died of typhoid fever. The vessels are in the muscular layer of an ulcerated portion of the ileum, the surrounding tissue being in a state of acute inflammation and the mucous layer having sloughed away. The vessels lie in an area of inflamed tissue and are surrounded by common round exudation

FIG. 51.—DISEASED AND NEW BLOOD-VESSELS IN THE WALL OF THE AORTA. (× 50.)

From a negro man fifty years old who died of endocarditis. The drawing includes the entire thickness of the adventitia and part of the muscularis. The vasa vasorum lie in the adventitia. Directly above the muscular tissue is a thick-walled vessel over which passes an arched string of fibrous tissue. Above this is another vessel which has been converted into an almost solid cord, for there is no opening in it but a small one at the side. Above and to the right of this is another thick-walled vessel with a small, laterally placed opening which contains some blood-corpuscles. It is impossible to be certain whether such vessels as these three are diseased vasa vasorum or if they are new vessels. There is at least one thin-walled vessel like a capillary which contains blood-corpuscles. It lies above and to the left of the middle one of the thick-walled blood-vessels.

FIG. 52.—DISEASED ARTERIOLE AND VENULE OF THE ILEUM. (× 240.)

From a woman twenty-six years old who died of typhoid fever. The vessels are in the muscular layer of an ulcerated portion of the ileum, the surrounding tissue is in a state of acute inflammation, and the mucous layer has sloughed away. *a* is the arteriole and *v* the venule. Neither of them has the appearance of ordinary blood-vessels,—the round cells of inflammation have invaded the walls of both. The calibre of the arteriole is nearly closed and its wall is very thick. The wall of the vein, on the other hand, is thin and composed of fibrous tissue and round cells.

FIG. 51.

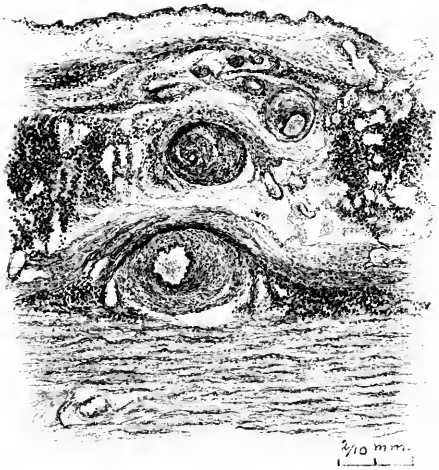
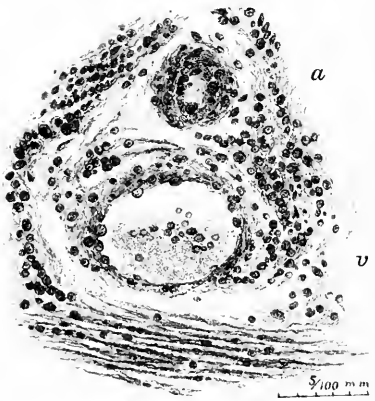


FIG. 52.



cells. Exactly similar ones are to be seen in the walls of the two blood-vessels, and the cells even project into the openings. The wall of the arteriole is very thick and its lumen is almost closed. The venule is structurally much more like a capillary than like an ordinary vein. Its wall is not composed of three layers—intima, muscularis, and adventitia—but of fibrous material containing cells. This fibrous tissue is like endothelium, but it is not disposed in a single layer as the endothelium of the capillaries of the smallest size is. The cells do not look as if they were swollen and rounded endothelial cells, but the appearance suggests that the inflammatory process had invaded the venule as well as the surrounding tissue, and that some of the cells in its wall are due to this invasion and are therefore of foreign origin. The processes of inflammation as they have been studied in living animals—in the cornea of the eye, for instance, and in the web of the frog's foot—are well known to pathologists. The changes of the rate of motion of the blood current, the clogging of the corpuscles in the vessels, and their passage through the walls of the capillaries which produces infiltration of the adjacent tissues, have all been seen and their various stages have been studied. Such studies have given an understanding of acute inflammation which is to a certain extent complete, but it has not as yet been possible to study chronic inflammation with anything like the same completeness, nor has any one in the same way seen the actual workings of inflammation upon human tissues.

Some of the effects of chronic inflammation upon human tissues are hard to explain by what has been learned from the study of experimental inflammation of the tissues of the lower animals, for such studies are necessarily confined, as has been said, to acute inflammation alone. The rest of my drawings which illustrate the condition of the blood-vessels in inflammation, in tuberculosis, and in syphilis are from the brain and spinal cord and their meninges. When tissues like the meninges of the brain and spinal cord are attacked by inflammation or by the tubercular process, the veins appear to be attacked earlier and to suffer more than the arteries. In sections of inflamed and tubercular meninges, the round cells can be seen in the walls of the veins when arteries lying near are almost normal. The arteries do become affected, but it seems as if they were attacked later than the veins. It is not at present known whether this is because veins are composed

of tissue of a loose texture and therefore they fall an easy prey to a process like cellular infiltration, while arteries—which are naturally of a firm and dense structure—resist the entrance of the cells into their walls, or if there is some other reason dependent upon the nature or function of the veins. The fact, however, is beyond question, and one of the most striking features of sections of inflamed and tubercular meninges is that the walls of the veins are infiltrated and their calibres obliterated by the cells, while the arteries remain much less diseased.

Fig. 53 is a picture of an artery and veins from the meninges of the spinal cord of a boy six years old who died of acute meningitis. The meningeal tissue around the vessels is inflamed. The artery is of nearly natural appearance upon one side, while on the other the round cells of inflammation have invaded it and lie close to it both upon its outer side and within its calibre. The veins are much more diseased than the artery. The most diseased vein, which is the one to the left, is almost closed by the cells, and the structure of its wall cannot be clearly distinguished, owing to the inflammatory infiltration which covers up and hides the natural tissue. The vein to the right is much less diseased. In conditions of inflammation like this, the veins are generally attacked earlier than the arteries and are more extensively diseased. This may be because of their structure, which is looser and more open, rendering their walls more easy of penetration by the invading cells. The process of disease represented by Fig. 53, which is purely inflammatory, cannot possibly be distinguished by its appearance from tubercular disease of blood-vessels.

Fig. 54 shows a group of blood-vessels of the meninges of the spinal cord of a negro woman twenty-five years old who died of tubercular meningitis, pulmonary tuberculosis, and gastric ulcer. The meningitis is said to be tubercular, because the woman had pulmonary tuberculosis, and not because of any peculiar appearance of the blood-vessels or of their surrounding tissue. The effect of the disease upon both the blood-vessels and the meningeal tissue is exactly similar to that produced by inflammation (see, for example, Fig. 53). The meningeal tissue is infiltrated with round cells, and the same process of disease has attacked the blood-vessels, which also are surrounded by the cells. The walls of the blood-vessels are more or less infiltrated. Of the four largest vessels that are included in the drawing, one is easily recognized as an artery and a second as a vein, but the two others are so altered

FIG. 53.—ARTERY AND VEINS IN INFLAMED PIA-ARACHNOID OF THE CORD. (× 50.)

From a boy six years old who died of acute meningitis. *a*, an artery, and *v*, *v*, veins. The tissue is infiltrated with inflammation cells, and the cells have forced themselves into the blood-vessels. The appearance suggests that the inflammation began in the fibrous tissue and then forced itself into the blood-vessels as it extended. The artery is hardly diseased upon the one side, and on the other the inflammation cells have passed entirely through its wall and some of them lie within its lumen. The veins are much more diseased than the artery. The one to the left is almost closed and its structure cannot be distinguished. In the vein to the right the disease is less extensive. This process of acute inflammation cannot be distinguished by its appearance from tubercular disease of blood-vessels.

FIG. 54.—BLOOD-VESSELS OF TUBERCULAR MENINGITIS OF THE CORD. (× 50.)

From a negro woman twenty-five years old who died of tubercular meningitis and pulmonary tuberculosis and gastric ulcer. *a*, *b*, *c*, and *d* are placed directly over four blood-vessels which lie in the diseased pia-arachnoid. *a*, an arteriole, and *b*, a venule; *c* and *d* are so much diseased that it is impossible to distinguish what kind of vessels they are. All four are infiltrated, and in all of them it looks as if the disease had originated outside and then invaded the blood-vessels rather than had its origin in the vessels themselves. The appearances of the tubercular disease of these blood-vessels are exactly the same as those produced by simple inflammatory meningitis. (See Fig. 53.)

FIG. 53.

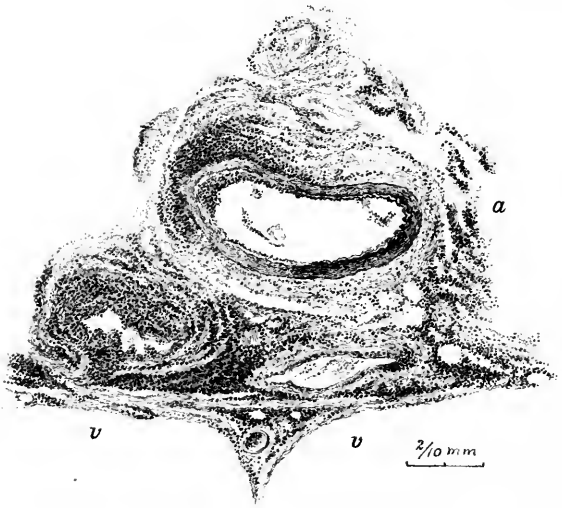
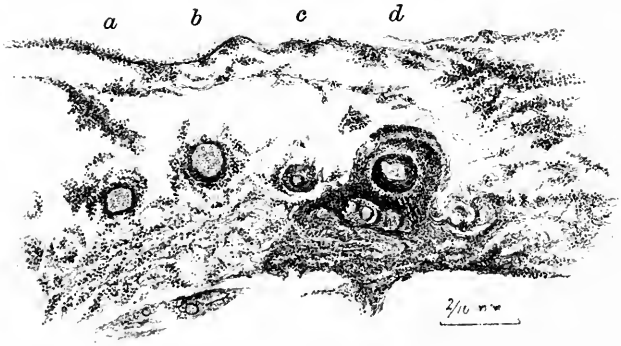


FIG. 54.



by disease that it is impossible to ascertain whether they are arteries or veins. This alteration of the natural characteristics of blood-vessels by disease, so that they cannot be recognized, is a common occurrence.

Figs. 55 and 56 depict an artery and a vein from a section of the spinal cord and meninges of the same patient as Fig. 54. As is the case in Fig. 54, the disease shown by Figs. 55 and 56 could not be recognized as tubercular had it not been that the patient had pulmonary tuberculosis. There is simply a cell infiltration similar in every respect to that which takes place in inflammation. The artery (Fig. 55) is surrounded with round infiltration cells, and the adventitia has been invaded by them so that it cannot be distinguished as fibrous tissue. The muscular coat shows no disease and is easily recognized. There are slight thickening and proliferation of the intima, and blood-corpuscles fill the greater part of the lumen. The vein (Fig. 56) is surrounded by round cells, and these have infiltrated it so that the tissue of the wall can be distinguished at only a small portion of the circumference. The disease has progressed much further in this vein than in the artery (Fig. 55) and the drawing gives a graphic and very correct impression of the effect which is produced by inflammation and tuberculosis upon veins. The cell infiltration has progressed so far that the vessel wall appears as if composed almost entirely of the exudate cells. There is hardly any distinguishable remnant of the natural tissue of the vein left.

Fig. 57 is taken from the same case as the three drawings last described. It is probably a vein, but of this it is impossible to be certain. The disease has progressed even further than in the vessels previously described. The surrounding tissue and the wall are overwhelmed by the cellular infiltration, and the lumen is nearly closed by the cells and clot. Clot, infiltration cells, vessel-wall, and the surrounding meningeal tissue are all blended into a single whole, of which the component parts cannot be distinctly recognized. The disease of this vessel could not have been known to be tubercular from its appearance alone, for the effect produced is exactly the same as that which so commonly results from inflammation. As has already been said of the three previously described drawings, the disease is only called tubercular meningitis because the patient had pulmonary tuberculosis. If such a thing be possible as a simple inflammatory meningitis in a person with pulmonary tuberculosis, this

case may well have been one of that kind. The lesions of the spinal cord and meninges are exactly similar to those found in cases of simple inflammatory meningitis. There was not a single miliary tubercle found anywhere, for the lesions of the lungs were not of that character, nor were there any miliary tubercles of the spinal meninges discovered.

Fig. 58 illustrates arteries and veins from the lumbar portion of the spinal cord of a negro man twenty-three years old who died of brain syphilis. There are one good-sized artery and two small arterioles, and two veins, one of which is much larger than the other. The arteries and veins are easily distinguished from each other by their appearances. Syphilis is supposed almost necessarily to produce alterations of the blood-vessels, and yet this group of vessels of the cord of a man who died of brain syphilis do not exhibit any greater departure from the standard of the normal than it is common to find in human beings even so young as twenty-three years of age. No disease of the blood-vessels of other parts of the cord nor of the brain of this man was found. The arteries (Fig. 58) might be said to be a little thicker walled than they should be, and in the larger one of them the intima is thicker upon one side than upon the other; but this imperfection, for imperfection it undoubtedly must be, is so common that it is difficult to find arteries of an adult without more or less of it. The veins are not distinctively diseased in any way. Their walls are not composed of three coats, as it is commonly taught that veins of this size are. They are formed of a loose-meshed fibrous tissue which is in many layers, and they are structurally much more like large and thick-walled capillaries than like ordinary typical veins. Such vessels, whether they be called veins or return capillaries, are very common. The striking feature which these vessels are intended to illustrate is, that in a case of syphilis the blood-vessels are nearly normal, although syphilis is the disease to which more than to any other endarteritis is supposed to be peculiar. I have not examined the blood-vessels in a very large number of cases of syphilis, but in those that I have examined, and there have been several of them, I have been surprised to find vascular disease absent.

The question to what degree the effects produced by the inflammatory process upon large arteries and veins resemble those produced upon capillaries, is an interesting one and is very important. The

FIG. 55.—TUBERCULAR INFLAMMATION OF AN ARTERY OF THE CORD. (× 50.)

From the same case as Fig. 54. There is infiltration of the tissue around the artery just as there is around the vein (Fig. 56), which is from the same section. The disease is much less extensive in the artery than in the vein.

FIG. 56.—TUBERCULAR INFLAMMATION OF A VEIN OF THE CORD. (× 50.)

From the same case as Fig. 55. Very little of the wall of the vein can be distinguished, for the cell infiltration is so great as to change it beyond recognition. The cells appear to be invading the wall of the vein from the outside, and the appearance suggests that the disease did not originate within the vessel but in the surrounding tissue.

FIG. 55.

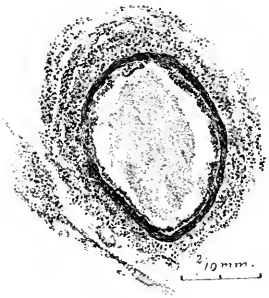
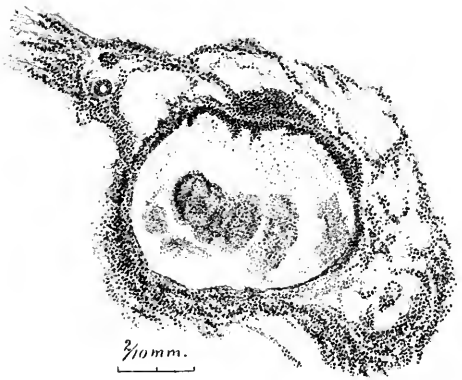


FIG. 56.



wandering of the corpuscles through the capillary walls, which has so often been watched in inflammation experimentally induced in the tissues of the lower animals, is well known, but it is impossible to believe that anything like it occurs in the case of the large arteries and veins which have thick walls of definite structure. It is unlikely that the blood-corpuscles pass through the walls of arteries and veins at all, unless possibly of those of the most minute size. A study of the appearances of the inflamed arteries and veins, of which drawings are included in this chapter, and of the blood-vessels of tubercular persons which are exactly similarly affected, drives one to the conclusion that these diseases attack the blood-vessels from without. The commonest known diseases of the arteries—and they occur in veins too, although much less frequently—are thickening and ulceration of the intima. These bear no resemblance to the lesions of inflammation and of tuberculosis shown by the drawings, but present a striking contrast to them. In the one case there is ulceration or thickening of the lining of the vessel, which produces a well-organized tissue of quite different appearance from normal intima. The whole process evidently has its origin within the vessel, and it often produces little or no change of the muscularis and adventitia, while in the other case the arteries and veins, if those included in this chapter and showing the diseases be accepted as fair types, look as if the diseases had attacked the blood-vessels from without. They are surrounded by infiltration cells and their outer coats are infiltrated. It is only in the smallest and thinnest-walled vessels that the infiltration has extended entirely through them, or that the cells lie within the lumen and obstruct it. The fact that vascular disease originates sometimes in the inner and sometimes in the outer coating of the vessels is one of the most striking things illustrated by the blood-vessels which are depicted in this chapter. It might be said that the vascular disease which attacks first the adventitia of the larger blood-vessels is not truly a primary disease of the blood-vessels, for it attacks them only through the vasa vasorum, which are distributed through the adventitia, or by a process of extension from the surrounding tissues. Such an objection is to a certain extent theoretically correct, but for practical purposes it may be assumed that vascular disease does arise in the two ways,—truly from within in endarteritis and in ulceration of the lining, and from without when such lesions

are produced as inflammation and tubercular disease of the blood-vessels.

Another curious and important lesson taught by such blood-vessels as those depicted by the drawings in this chapter, is that the three diseases, inflammation, tuberculosis, and syphilis, all produce lesions which are in no way peculiar to them nor to any other one disease. Any of the lesions illustrated may be produced by other diseases besides the one with which the patient from whose body the specimen was obtained was suffering. Inflammation and tuberculosis produce lesions which are histologically identical, and the lesions found in the case of syphilis—and I have found identical ones in other cases—are those which are common to all sorts of diseases in human beings, and even in those who have not seemed during life to be diseased at all—for instance, in persons who have died of violent death, having been previously in apparently good health. My own experience in the examination of the tissues of persons who were known during life to have had syphilis, and even of those who died of its direct effects, leads me to think that syphilis does not so often cause disease of the blood-vessels as has been thought by some eminent authorities.

CHAPTER VIII

The Blood-Vessels of the Heart

The heart is certainly one of the most important organs of the human economy if it is not the most important of them all. It is therefore hardly necessary to say that it is impossible to know its anatomy too thoroughly. I have already issued various publications upon the subject of the blood-vessels of the heart, but at the risk of repetition I shall try to describe the entire course of the cardiac circulation as far as it is known. In some of my publications previously issued, it was asserted that the arteries and veins upon the surface of the heart are like those of the other organs, and that they are composed of three coats. This is strictly correct as far as concerns the arteries, and almost equally so in regard to the veins ; but a more extended study of the subject, carried out since my last publication was issued, has made me think it necessary to modify the statement a little. The veins upon the surface of the heart do indeed ordinarily have three coats,—intima, muscularis, and adventitia,—but sometimes they are formed of a single coat, and the tissue composing this coat appears to be fibrous, and no muscle cells can be distinguished in it. Whether this results from disease only or can occur also in the normal heart I am not now certain.

The sinus venosus—which is the terminal vein of the heart, and is therefore the largest of the cardiac veins—is composed, as far as I have been able to discover, of fibrous tissue only (see Fig. 17). This fibrous tissue is directly in contact with the cardiac muscle. The arterioles of the heart are very short after they leave its surface to penetrate the muscular tissue, breaking up almost immediately into capillaries. The capillaries surround the muscular fibres in every conceivable way and run in all directions amongst them—parallel with them, across them at right angles, and diagonally at all possible angles. The number of the capillaries is very great, showing that the heart is most bountifully supplied with blood. The capillaries of the heart, however, are not simply distributed around the muscular fibres, as those of the kidney surround the tubules, but they actually penetrate the

fibres. The fact that the muscular fibres of the human heart are penetrated by the capillaries is striking and curious and there is no such penetration at an early embryological stage; but the subject is one that I have already discussed.[1] Another striking feature of the blood-vessels of the heart is the existence of many very large capillaries. These are so large and so numerous and of such curious shapes sometimes that it would seem that they must serve as reservoirs besides being carriers of blood, resembling in this respect the venous sinuses of the placenta.

In a study like this of the blood-vessels of the heart, it might for some reasons be best not to attempt to discuss the subject of the structure of the muscle. On the other hand, the blood-vessels are so intimately related to the muscular tissue that it is impossible to comprehend their minute anatomy without knowing something of that of the muscle. The involuntary muscle of the human heart is different from other involuntary muscle and is different from voluntary muscle also, but heart muscle is much more nearly like voluntary muscle in appearance than like ordinary involuntary muscle. The fibres of the muscle of the heart are branched, and it has been said that they are without any sheaths like the sarcolemma of the voluntary muscle. The appearance of the cross striæ which are sometimes so very distinct, and of the longitudinal markings, which have been explained as being due to the division of the fibres into fibrillæ, are well known, and so are the familiar elongated cells with nuclei and pointed ends of common involuntary muscle. When one comes, however, to consider the minute structure of the striped voluntary muscle of man, or of the lower animals, or the muscle of the human heart, it must be confessed that there is not much known about it. It is not yet known how any muscle performs its function of contraction, and until more has been learned of this important physiological question it is likely that it will continue to be impossible to know what the structure of muscle is.

Various theories have been put forth to explain muscular contraction, but no one of them has as yet been established. There cannot be anything incomprehensible about it, and probably the contraction of muscle is caused by some mechanical principle as simple in its

[1] Origin of Disease, by Arthur V. Meigs, second edition, page 65: J. B. Lippincott Co., 1899.

nature as the force of steam pressure or that which is derived from the descent of water from a higher to a lower level. The sooner scientific men divest themselves of the belief that there must be something complicated or inexplicable about muscular contraction and search for a simple cause, the sooner a solution of the problem will be found. Within a few years it has been suggested that muscular contraction is caused by the movement of fluids. That by the process of imbibition fluid moves from around certain portions of muscle to the interior, and that the enlargement of the muscle caused by this imbibition of fluid causes the muscle to shorten. McDougal has published essays[1] in which he endeavors to prove the correctness of the imbibition theory. His experiments were made principally with the wing muscles of insects, and his conclusion is that the fibrillæ are the units of contraction. He states that each fibrilla has partitions across it, and that there is an interfibrillar fluid. When contraction takes place interfibrillar fluid passes to the inside of each one of the separate spaces of the fibrillæ, and this causes widening and thereby contraction. He gives an interesting demonstration and proves by calculations that, if the fibrillæ of muscle have a certain structure, contraction may take place in the manner he suggests. Further he says that he has seen with the microscope lateral bulgings upon the sides of the fibrillæ when they are contracted. These lateral bulgings have been seen and described by quite a number of different observers. They have sometimes been called waves of contraction.

Edward B. Meigs has reached conclusions in some respects similar from studies carried out principally upon the voluntary muscle of the frog,[2] but he believes that the unit of contraction is the muscle fibre and that in the frog fibrillæ do not exist as they are commonly described. This conclusion is supported by mathematical calculations demonstrating that, if the muscle fibre of the frog has the structure that he predicates, and fluid is imbibed, contraction must take place.

[1] W. McDougal, On the Structure of Cross-Striated Muscle and a Suggestion as to the Nature of its Contraction, Journal of Anatomy and Physiology, vol. xxxi, page 410, 1897; and A Theory of Muscular Contraction, Journal of Anatomy and Physiology, vol. xxxii. page 187, 1898.

[2] Edward B. Meigs, On the Mechanism of the Contraction of Voluntary Muscle of the Frog, American Journal of the Medical Sciences, April, 1904; and A Mechanical Theory of Muscular Contraction and some New Facts Supporting it, American Journal of Physiology, vol. xiv., No. 11, page 138, 1905.

There is a description with illustrations showing that the appearance of the voluntary muscle of the frog is very different according as it is examined contracted or uncontracted. Uncontracted muscle fibre presents the appearance of a cylinder with straight sides, while the same fibre when contracted has bulgings along its sides which make it resemble a string of beads. There are illustrations to show that there are partitions across the muscle fibres at regular intervals, that the outer portions or sheaths of the fibres are quite different in structure from the central part, and that the peripheral and central parts of the fibres appear very different according as the muscle is examined contracted or uncontracted.

The opinions of the one observer that the fibrillæ and of the other that the fibres are the contractile units are not necessarily irreconcilable, for it may be that what are called the fibrillæ of the wing muscles of insects, and which are capable of such exceedingly rapid contractions, are the same as what are called fibres in the voluntary muscle of the frog. This imbibition hypothesis for the explanation of the contraction of muscle appeals to me as more reasonable than any other of which I have heard, and it is supported by strong evidence. In my own examinations of human heart muscle I have found many conditions that I cannot comprehend if the commonly accepted belief that the fibres are regularly divided into fibrillæ is correct. It is invariably the case that the central parts of the muscle fibres of the human heart, especially the portions of the centres near the nuclei, differ in appearance from the outer parts. It has been said that the centres are more or less hollowed out, which is a way simply of saying that the liquid or solid substance that occupied the centres of the fibres did not stain like the outer portions. This so-called hollow condition of the fibres has generally been attributed to disease, but, as it is so invariably present in human heart, I have long been disposed to believe it to be, partly at least, natural. Such an appearance as that of Fig. 53 in my book on the "Origin of Disease," which shows human heart muscle that is hollow in the centre and has a peripheral part or sheath like ordinary human heart muscle, seems to me to support the imbibition hypothesis which is founded upon the existence of a great difference between the peripheral and central parts of the muscular fibres.

The fact that there is a difference between the peripheral and central

parts of the muscular fibres, especially of those of the human heart, has been recognized by histologists. For instance, Piersol,[1] in describing heart muscle, says, "The peripheral fibrillæ are grouped into flat ribbon-like muscle-columns, somewhat radially disposed about the circumference of the fibre; the remaining central portion is occupied by prismatic bundles of fibrillæ, together with the nuclei and the associated protoplasm (Ranvier, Kölliker)." This shows that it is pretty well known that there is a difference between the peripheral and central portions of the fibres, but the description that has been quoted is not very clear, and it betrays the fact that, while it has been reorganized that the outer and inner portions of the fibres are different, the nature of the structure of muscle is not yet known. It might be thought, as I have already said, that the subject of the minute anatomy of the heart should not be considered in a study of the cardiac blood-vessels; but it is impossible to have full knowledge of the blood-vessels until the structure of the muscle is better known than it now is, and it is most probable that the next step in advance will be the acquisition of an understanding of muscular contraction which will necessarily bring with it a better knowledge of the anatomy of the muscular fibres. Everything about anatomy cannot be learned from embryology, for it is certain that there are conditions of structure which are post-embryonic in their development. For instance, it is reasonably certain, from what is known of the mode of development of muscle, that at early embryological periods the muscular fibres of the heart are not penetrated by the capillaries, but I believe that there can be no doubt that they are so penetrated in the adult man. This must be a post-embryonic development, and the only reasonable hypothesis for its explanation is that the capillaries become surrounded by a process of inclusion—that subsequent to birth the muscular tissue grows around the capillaries. The discovery of the cause of muscular contraction is almost certain to throw light upon the whole subject, and many of the already ascertained facts in regard to the structure of muscle seem to me to point to the probability of the correctness of the imbibition hypothesis.

The illustrations with this chapter exhibit the peculiarities of the blood-vessels of the heart in a way that it is impossible to equal by any verbal description. Figs. 59, 60, 61, and 62 are four drawings of

[1] Normal Histology, by George A. Piersol, page 66: Philadelphia, J. B. Lippincott Co., 1893.

heart, and they are intended to show the most striking features of the minute cardiac blood-vessels as they enter the muscular tissue, ramify in it, and come out from it. It is the heart of a negro woman forty years old who died from the effects of burns. Some pieces of the organ were preserved in Flemming's solution, and others in seventy per cent. alcohol, and they were stained in bulk with borax-carmine and embedded in paraffin. Fig. 59 is a terminal arteriole in the muscular tissue. It shows the branching of the arteriole and the change into capillaries. This conversion is effected by the disappearance of the adventitia and of the muscular tissue. At one of its ends the vessel is a minute artery with three coats, and at the other it has divided into capillaries consisting of a single layer of endothelium. Between these two extremes is seen the gradual disappearance of the adventitia and muscularis. Scattered muscular fibres both of the longitudinal and of the circular layers and how these become more and more sparse are well shown by the drawing. The manner in which arteries divide and subdivide to form capillaries is perfectly well known, but it has not been well shown by illustrations so often as to make this one of mine seem trite.

Fig. 60 illustrates muscular fibre in cross-section. It shows the capillaries in various situations. They are seen in the intermuscular spaces and in the fibres themselves, so that they are completely surrounded by muscle. Some of the capillaries within the fibres are simply rings of endothelium (*b* and *d*), and others (*a* and *c*) are composed of endothelium with a nucleus at one side, producing an appearance somewhat like that of a seal ring. This drawing has been so carefully elaborated that the peculiarities of the appearance of the muscular tissue and of the capillaries can be even better distinguished if it is examined with a magnifying glass.

Fig. 61 shows heart muscle fibre cut longitudinally. At one side a group of capillaries is seen entering the muscle to be distributed among the fibres. It is a good illustration of the great number of the capillaries and of the manner in which they pass between and around the fibres. In this case no capillaries can be distinguished within the fibres, but it is always more difficult to see capillaries within the fibres in longitudinal sections than when the muscle is cut across.

Fig. 62 is reproduced from a drawing of a large capillary. It is impossible to be certain whether any one particular large capillary like

FIG. 59.—TERMINAL ARTERIOLE OF HEART. (× 55.)

From a woman forty years old who died of burns. Most of the muscular fibres are cut longitudinally. The arteriole is branched and it extends across an intermuscular space. To the right it presents the common appearances of an arteriole; the involuntary muscular tissue is easily distinguished. To the left the small terminal branches are capillaries. The manner in which arterioles break up into capillaries is very well shown. The two outer coatings—adventitia and muscularis—become thinner and thinner until they disappear and only the intima remains, which is the endothelium, and it forms the wall of the capillary.

FIG. 60.—HEART CAPILLARIES. (× 260.)

From the same case as Fig. 59. The muscular fibres and the capillaries are cut across. The fibres are of very irregular shapes. The capillaries are in the spaces between the fibres and in the fibres, some capillaries being in the very centres of fibres. *a*, a capillary in the centre of a fibre. Its endothelial wall is distinctly shown, and upon one side the nucleus has been cut through, and as this makes a thickening upon one side it gives the capillary the appearance of a seal-ring. *b*, a capillary in the centre of a fibre,—it is a delicate ring of endothelium which is nearly circular. *c*, a capillary in a space between fibres. A nucleus was cut through and the capillary therefore looks like a seal-ring. *d*, a capillary between fibres. It is a delicate circle of endothelium.

FIG. 61.—HEART CAPILLARIES. (× 260.)

From the same case as Fig. 59. The muscular fibres and the capillaries are cut longitudinally. To the right a number of capillaries are seen entering the heart-muscle. They pass in among the fibres and in some places they can be seen crossing the fibres at various angles, and again they are shown between fibres and parallel with them.

FIG. 62.—LARGE RETURN CAPILLARY OF THE HEART. (× 55.)

From the same case as Fig. 59. The muscular tissue is cut longitudinally. The greater part of the large return capillary lies in an intermuscular space. A number of branches, some of which are seen to be coming out of the muscular tissue, join to form the main tube. The walls of all of these vessels are composed of endothelium, although the largest one is of greater size than the arteriole shown by Fig. 59. The venous radicles in the muscle of the heart are almost all of this nature, and it is unusual to find a vein with three coats anywhere in the heart except upon the surface.

Fig. 59

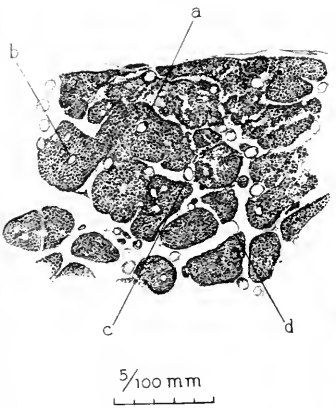


Fig. 60

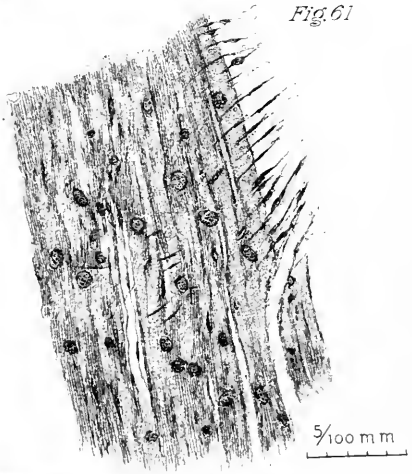


Fig. 61

Fig. 62

this was afferent or efferent in its function, or if it was of the nature of a sinus. The fact, however, that after death such vessels are much more frequently found to be filled with blood-corpuscles than the arterioles are, and that practically there are no veins within the muscular tissue of the heart, makes it certain that some of the large capillaries are efferent in function and do the work of veins. The blood-vessel which is here depicted I believe to be a good type of this class. It may be thought strange perhaps that in a plate like this, which represents heart muscle, no attempt has been made to show the cross striæ which are commonly supposed to be among the most striking features of the appearance of heart muscle, as indeed they are. The cross striæ of muscle, and especially of human heart muscle, are, however, by no means so easy to see as is commonly supposed, and they are very difficult to depict. It is commonly the case that in such human heart muscle as can be obtained for microscopical examination the cross striæ cannot be seen at all, and the fibres have instead a rather granular appearance. Cross striæ can be seen in places in the muscle depicted by the plate, but only in small areas and by careful focussing of the microscope, and the muscle, if its general effect be considered, has much more nearly the appearance which is shown by the drawings than would have been produced if lines had been drawn across the fibres to represent the cross striæ.

This plate gives an excellent general idea of the cardiac circulation in the muscular substance of the heart. The blood enters by arterioles and is distributed by capillaries, which exist in vast numbers, among and around the muscular fibres and even in their very centres. It then comes out through large capillaries which perform the function which is carried on by minute veins in other organs.

Fig. 63 represents the heart of a man thirty years old who died of lead encephalopathy. At the time the autopsy was made the arteries were injected with a solution of Berlin blue, and afterwards the tissue was stained in bulk with borax-carmine and embedded in paraffin. The injected material passed into the capillaries, and the illustration, which was made with the camera lucida and drawn accurately to scale, shows that the vascular supply of the heart is very rich. It must be remembered that it is most unlikely that even half of the capillaries are filled with the blue injection material. The drawing shows many capillaries that appear to cease abruptly, and

there are spots that are entirely uninjected. It is reasonable, therefore, to believe that my estimate that more than half of the capillaries are uninjected is not exaggerated. The number of capillaries in the heart, therefore, is even greater than this drawing would lead one to suppose; but upon the whole it gives an excellent general idea of the capillaries of the human heart.

Fig. 64 is from the heart of a man sixty years old who died of endocarditis and cardiac dilatation. It was injected and prepared exactly as was Fig. 63. The muscular fibres are cut longitudinally, and in one of them there is an injected capillary running directly in the centre of the fibre which is most graphically shown. In other respects the illustration shows the ordinary appearances of cardiac muscular fibre and the relations of the capillaries to them. The capillaries are colored blue and can be seen branching in various directions. Most of them lie between the fibres.

Fig. 65 depicts the heart of a man forty-six years old who died of tuberculosis. This heart was injected and prepared in the same manner as the one represented by Fig. 63. The muscular fibre is cut across and most of the capillaries are seen in cross-section, although a few, especially some of the larger ones which are entering from the pericardium, are cut lengthwise. Most of them are in the intermuscular spaces, but quite a number are more or less completely within the muscular fibres. Two capillaries (*d*) lie completely within a fibre. These two capillaries are not completely filled by the blue injection which must have passed through them and tinted them; they demonstrate, therefore, unusually well that the capillaries penetrate to the centres of the fibres. Their endothelial walls and the nuclei to one side can be easily distinguished. Injected preparations are not generally the best in which to study fine points in histology, for the injection material usually fills the capillaries full and the mass of color obscures the vessel-walls so that only the situations and not the characteristics of the capillaries can be seen. In this case the injection passed into the vessels and stained them delicately, but they are not filled and their walls can therefore be distinctly seen.

Fig. 66 shows a capillary of the heart of a woman forty-two years old who died of cerebral apoplexy. The shape is very curious and there cannot be any doubt that it is a capillary, for the appearance of the wall is perfectly characteristic and the interior is partly filled with

FIG. 63.—INJECTED BLOOD-VESSELS OF HEART. (× 55.)

From a man thirty years old who died of lead encephalopathy. The heart-muscle is cut longitudinally and it is stained red. The blood-vessels are blue, and it is seen that they are very numerous, although it is almost certain that only a small proportion of the total number of them show, for it is reasonably sure that the blue injection material failed to fill them all. The supply of blood to the heart is very bountiful.

FIG. 64.—INJECTED CAPILLARIES WITHIN THE MUSCULAR FIBRES OF THE HEART. (× 260.)

From a man sixty years old who died of endocarditis and cardiac dilatation. The muscular fibre is cut longitudinally. It is red and the injected capillaries are blue. They lie between the fibres and within them. In the middle portion of the drawing is a broad fibre, and in its very centre is an injected capillary.

FIG. 65.—INJECTED CAPILLARIES WITHIN THE MUSCULAR FIBRES OF THE HEART. (× 260.)

From a man of forty-six years who died of tuberculosis. The muscular fibre is cut across. It is stained red and the injected capillaries are blue. The fibres are of irregular shapes and of varying sizes. The section includes a portion of pericardium and there are two good-sized blood-vessels extending from it into the muscular tissue. These were cut longitudinally. Most of the capillaries were cut across and lie between the muscle-fibres and within them. *d* shows two capillaries within muscular fibre. They were cut across and a nucleus is seen in each of the capillaries, which makes them look like seal-rings. The injection did not fill these capillaries and they are only slightly tinted blue. In consequence of this the structure of the vessel walls and the nuclei can be better seen than in most injected blood-vessels, for heavy injections obscure the tissues.

Fig. 63.

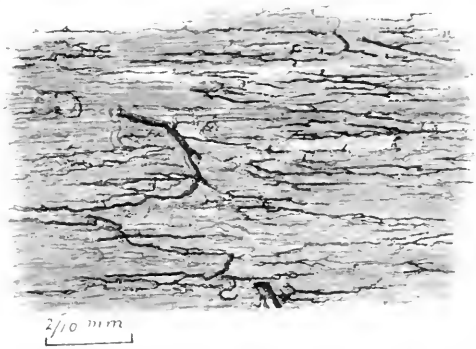
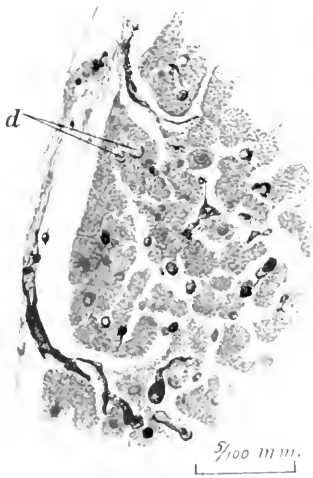


Fig. 64.

Fig. 65.



blood-corpuscles. There is no reason to suppose that this blood-vessel is abnormal, and if it is not it must have fulfilled the function of a reservoir rather than of a mere carrier of blood, for if its only use had been to transport blood it would not have been of such great diameter when the entering tube is so small. This exemplifies a curious and, as far as I know, not commonly described phase of the cardiac circulation.

Fig. 67 is a group of capillaries of the heart of a negro woman twenty-eight years old who died of catarrhal pneumonia. It shows how very numerous capillaries are in the heart, and there is no reason to suppose that these are an abnormal production. The muscular fibres, however, are separated in a manner that is probably abnormal. This may be due to the growth of fibroid tissue, or there may have been œdema, the exudation causing separation of the fibres. The group of capillaries affords a striking example of how very vascular the heart is.

In Fig. 68 is seen a group of blood-vessels consisting of an artery and two veins of the surface of the heart of a man forty-six years old who died of pulmonary phthisis. The vessels lie in the fat upon the surface of the heart. No one of these blood-vessels is normal. The wall of the artery is thickened more at some parts of its circumference than at others. The intima is relatively much more thickened than either of the other coats. The veins are quite unlike the accepted histological standards. Their walls are of irregular thickness and are formed of loose-meshed tissue composed of involuntary muscle and connective tissue. There is no distinct separation into three coats. As already said, it is very difficult to find blood-vessels which are typically normal according to the accepted standards of anatomy. Embryologists have elaborately studied the development of the blood-vessels in many of the lower animals, and to a great extent in man, and an accepted and correct standard of the normal has been attained ; but the study of human tissues obtained post mortem from the bodies of persons, almost all of whom have died of disease, shows that it is rare to find blood-vessels that are absolutely normal. The condition of these three vessels is fairly typical of what it is common to find in the hearts of persons dead of almost every known disease. In the heart it is common to find the intima of the arteries greatly thickened, and the veins upon the surface are often composed of loose-meshed tissue

and without any distinct division into three coats. In order to see the more minute details of such disease it is necessary to use greater amplification, but the drawing gives a good general idea of the condition.

Fig. 69 is an illustration of an artery of the surface of the heart of a negro infant one year old who died of chronic catarrhal pneumonia. It shows that even at so early an age the intima may not be simply a layer of endothelium lying inside the plicated membrane. At the lower portion in the picture the intima is cellular and it is slightly thickened, and the plicated membrane at this point is almost indistinguishable. This I believe to be the earliest form of disease of this nature. The subject has already been discussed in my book on the "Origin of Disease" (page 43). Fig. 70 depicts an artery of the surface of the heart of a boy two years old who died of nephritis. It shows disease of the same nature as that seen in Fig. 69, but very much more extensive. The adventitia shades into the surrounding fibro-fatty tissue so that its boundaries cannot be distinguished. The muscular coat is of varying thickness at different parts of the artery, and this must be due to disease. The plicated membrane is sharply outlined and is easily seen at most places, but at some parts of the circuit it disappears into the intima, which is everywhere thicker than normal and is irregularly thick. A more typical example of the condition commonly found in the arteries of the human hearts obtained post mortem, it would be difficult to discover. It is rare to come across an artery that answers the ordinary descriptions of the normal, and very common to find vessels like this one. It is almost certain, therefore, that the normal type is seldom to be found long after birth. I do not think I shall exaggerate in saying that it is not generally known that the arteries are often like this even at so early a period of life.

Figs. 71 and 72 show blood-vessels of the heart of a woman forty-seven years old who died of obstruction of the bowel. They lie very close together in the tissue. Fig. 71 is probably an efferent vessel of the character which has already been described (Fig. 62). It is not exactly like the ordinary small capillaries, for it is thicker walled, not being composed of a single layer of endothelium, and it contains more cells than are ordinarily present in the walls of capillaries. It is probably a fair type of the kind of vessels that take the place of veins in

FIG. 66.—NORMAL LARGE CAPILLARY OF THE HEART. (× 105.)

From a woman forty-two years old who died of cerebral apoplexy. The capillary resembles a wine-flask with a narrow neck. Blood-corpuscles lie within it. Below, to the left, and above, the capillary wall containing endothelial nuclei is distinct. To the right there is no capillary wall visible. At the top the capillary divides into two branches.

FIG. 67.—NORMAL CAPILLARY NET OF HEART. (× 240.)

From the heart of a negro woman twenty-eight years old who died of catarrhal pneumonia. The capillaries are easily recognized. A good many of them contain blood-corpuscles. The muscular fibres are somewhat widely separated,—this was probably caused by the deposit of fibrous tissue or by œdema of the heart.

FIG. 66.

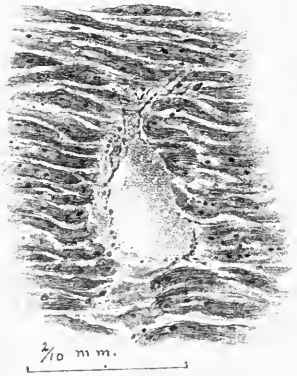


FIG. 67.

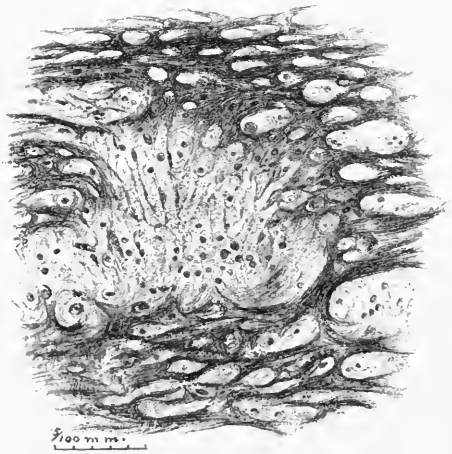


FIG. 68.—THICKENED ARTERY AND DISEASED VEINS OF THE HEART. (× 8.)

From a man forty-six years old who died of phthisis. An artery and two veins in the fat on the surface of the heart. The artery lies between the two veins. Its walls are thickened, especially the intima. The veins are quite unlike the accepted histological standards, for their walls are principally made up of a loose-meshed tissue composed of involuntary muscle and connective tissue, and there is no distinct separation into three coats. Such disease of arteries and veins is common in those who have had chronic disease and in persons past middle life.

Fig. 68.

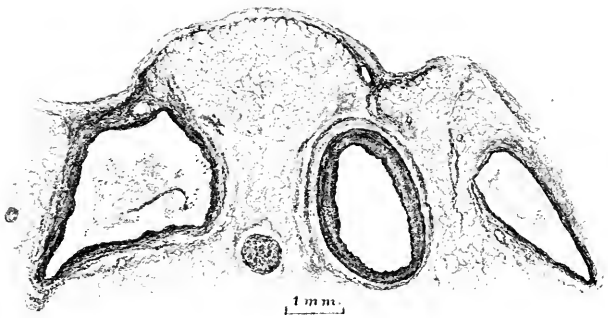


FIG. 69.—ARTERY OF THE HEART; NEARLY NORMAL. (× 50.)

From a negro infant one year old who died of chronic catarrhal pneumonia. The artery is nearly normal. The intima is a little thick and the plicated membrane indistinguishable at the lowest part.

FIG. 70.—DISEASED ARTERY OF THE HEART. (× 50.)

From a boy two years old who died of nephritis. The artery lies upon the surface of the heart, and at so early a period of life the heart has very little fat upon it. The muscular coat is of different degrees of thickness at different parts of its circuit. The plicated membrane is distinguishable around most of the artery, but not all. The intima is thickened, showing that this condition, which is almost universal in older people, may occur in early life.

FIG. 69.

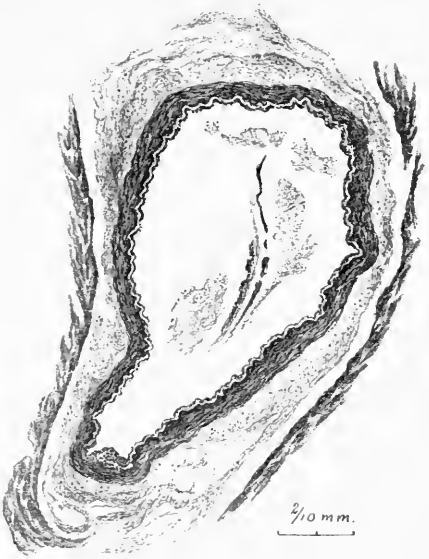


FIG. 70.

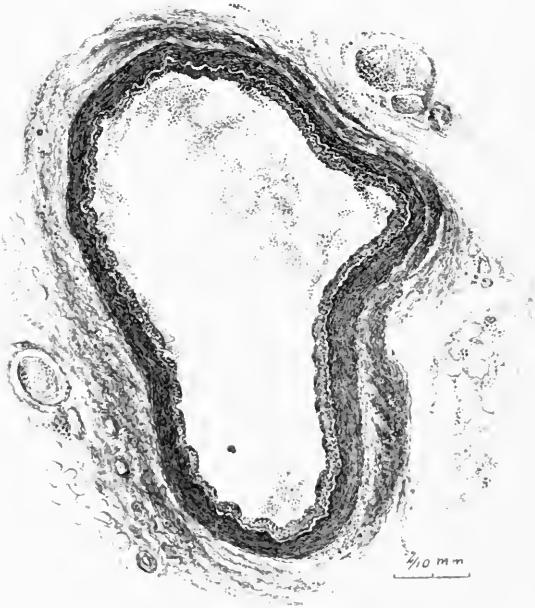


FIG. 71.—NORMAL BLOOD-VESSEL FROM HEART. (× 105.)

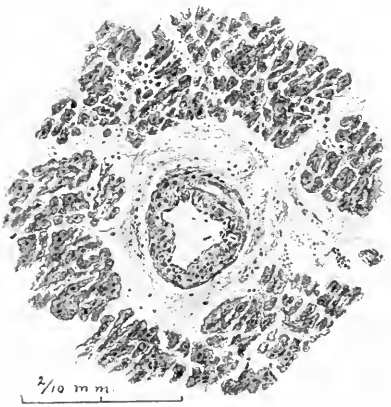
From a woman forty-seven years old who died of obstruction of the bowel. Blood-vessels like this are generally found in human heart. This vessel has not the characteristics of arteries or veins, nor is it exactly like the accepted descriptions of capillaries, for it is thicker-walled. The wall is not composed of a single layer of endothelium, for it contains more than one fibrous layer and quite a good many cells which do not answer the description of endothelial cells. The vessel has some small normal capillaries around it, and muscular fibres, most of which have been cut across.

FIG. 72.—DISEASED BLOOD-VESSEL OF THE HEART. (× 105.)

From the same case as Fig. 71. The vessel is probably a vein. The walls are thickened so that the tissue hangs in festoons in the lumen. This tissue is rich in cells and looks much more like epithelium than like the ordinary tissue of blood-vessel walls.

FIG. 71.

FIG. 72.



the substance of the heart. Fig. 72 is probably a vein. The muscularis is loose-meshed and it is like that shown by Fig. 34, and inside this is a tissue which is unlike any of the material which forms normal blood-vessels. It is more like epithelium than like any ordinary vascular tissue. I have already described somewhat similar growths in blood-vessels.

Fig. 73 shows a vein of the surface of the heart of a man twenty-seven years old who died of acute cholera morbus. There is extensive blood infiltration and many of the fat-cells of the fatty covering of the heart, in which the vein is situated, are filled with blood-corpuscles which had exuded from the vascular channels. These show distinctly under greater amplification. The wall of the vein is greatly thickened and this thickening is of very irregular distribution, being much greater in some places than in others. The thickening seems to be principally of the intima, which is unusual in veins although common in arteries. Altogether the condition of disease is a difficult one to explain, for it is not common in my experience to find veins like this, and besides it is almost necessary to believe that the disease must have been a chronic and latent one which preceded the acute attack of cholera morbus of which the man died and which lasted only twenty-four hours. To the fact that latent chronic disease is common in persons supposed to be healthy and who die of acute attacks, I have frequently alluded. Fig. 74 shows a vein upon the surface of the heart of a woman twenty-five years old who died of puerperal septicæmia. It can hardly be thought that this vein is normal, and yet it is difficult to say exactly what has affected it. It is thicker walled than normal and there is no division into three coats, the greater part of the tissue composing it seeming to be fibrous. The artery accompanying this vein is greatly diseased and its intima is very much thickened. It is likely that in the case of this vein, as well as in that of Fig. 73, there was latent chronic disease which preceded the final fatal attack which was of short duration. Fig. 75 depicts another vein and an artery of the surface of the heart of the man from whom the vein shown by Fig. 73 was obtained. The vein is thicker walled than the artery and there is no differentiation into three coats. The condition is certainly one of disease, but it is impossible at present to give an exact explanation of it. Perhaps the blood effusion in the fatty covering of the heart, which was so exten-

sive in the case and which is shown by the drawing, may have caused something of the nature of œdema of the wall of the vein. The accompanying artery is not affected in a corresponding manner, but the tissue of arteries is much denser than that of veins, and, being composed of material of looser texture than arteries, the veins are probably more liable to become swollen and unnatural in appearance.

It may be well to sum up some of the more important points touching the blood-vessels of the heart that have been under consideration. It is almost certain that, with the acquisition of knowledge of the nature of the force that causes the contraction of muscle, there must come an advance in knowledge of the minute anatomy of muscular fibre, and therewith a corresponding advance in knowledge of the capillaries of the heart and of their distribution. What has been said in this chapter shows that it may be hoped that something will soon be learned regarding the cause of muscular contraction, and enough has been said to show that the belief which is so prevalent, that muscular fibre is a nearly homogeneous substance, is far from being correct. Histologists know that there is a great difference between the peripheral and central parts of the fibres.

The blood-vessels of the heart have striking peculiarities of their own, and are in several ways different from those of the other organs. The illustration of a terminal arteriole, and of its breaking up into capillaries, is interesting. Not many illustrations of vessels like this are to be found in books, although there must be thousands of such vessels in all human beings. It has been shown that the accompanying venous radicles of the small arterioles of the heart sometimes have the structure of large capillaries, and one of the illustrations shows that the venous capillaries are sometimes so large as to make it likely that they must have something of the function of reservoirs like sinuses. The fact that minute arterioles are accompanied by large capillaries instead of by veins is known by anatomists to be the arrangement in various parts of the body, but it is not as generally understood as it should be. The penetration of the muscular fibres of the heart by the capillaries is an anatomical peculiarity that I have dwelt upon much. What is known of embryology seems to prove that there cannot be any capillaries within the fibres during the earlier stages of development of muscle, and there is at present but little known of postnatal development. The discovery of the capillaries within the muscu-

FIG. 73.—DISEASED VEIN OF HEART. (× 50.)

From a man twenty-seven years old who died of cholera morbus. A vein in the fat upon the surface of the heart. Extensive infiltration of blood into the fat had occurred and many of the fat-cells around the vein are seen to be full of red blood-corpuscles. The vein itself has greatly thickened walls, and this thickening is very irregular, being twice as great above as it is below. The wall is thrown into folds, which is due to post-mortem shrinkage. The thickening of this vein is of rather unusual nature,—it looks as if there was great increase of the intima, which is common in arteries but not in veins.

FIG. 73.

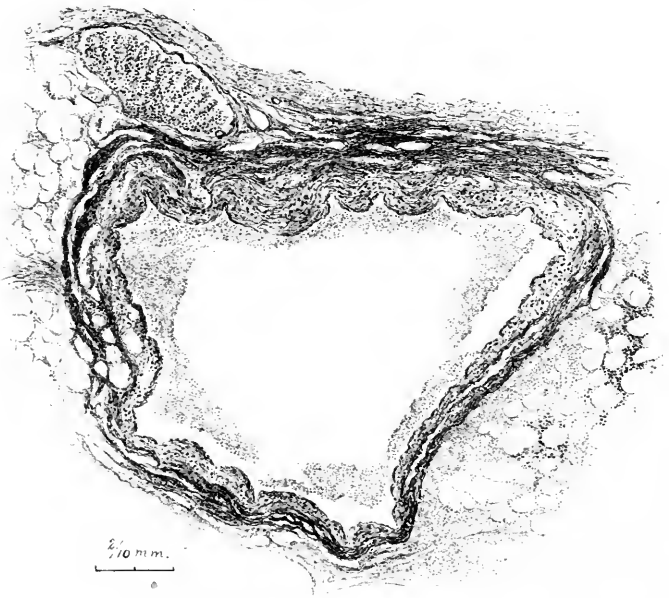


FIG. 74.—VEIN OF THE HEART. (× 50.)

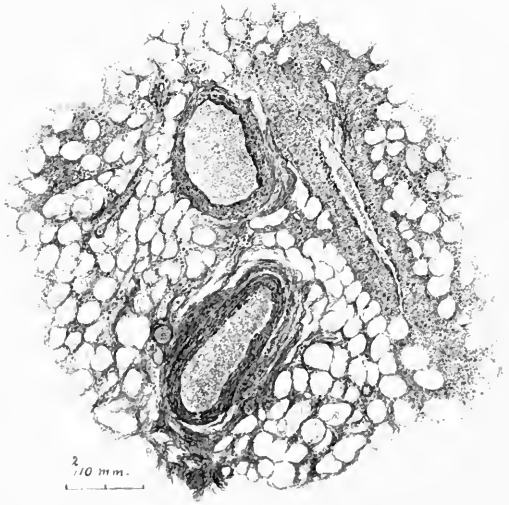
From a woman twenty-five years old who died of puerperal septicæmia. The vein is in the fat upon the surface of the heart. It is diseased, for the wall is thicker than natural and there is no division into three coats, and no tissue which is distinctly muscular. The artery accompanying this vein is quite extensively diseased, the intima being very much thickened.

FIG. 75.—ARTERY AND DISEASED VEIN OF THE HEART. (× 50.)

From a man twenty-seven years old who died of cholera morbus. The artery is below and the vein above it; they both lie in the fat with which the heart is covered. There is extensive infiltration of the fat with blood; this is so great that many of the fat spaces are filled with red blood-corpuscles. The vein (the upper vessel) is quite unlike the accepted standards of the normal. Its walls are thicker than those of the artery, and there is no distinction into three coats. It is somewhat like Fig. 34 and other veins diseased in the same way.

FIG. 74.

FIG. 75.



lar fibres of the heart is as yet inconclusive, but I do not think there can be any reasonable doubt of the fact. Nothing can now be said of its cause except that it is probably the result of a process of inclusion, the fibres growing around the capillaries after birth, or possibly the development takes place during the latter parts of the intra-uterine period.

The injected specimens of heart of which colored illustrations are included in this chapter make a beautiful and most graphic demonstration of the capillaries within the muscular fibres. I was many times urged to make injections of the heart to show the distribution of the capillaries, and the injected preparations are very pretty, and they make it easy to see the capillaries within the fibres, but they do not show anything that I had not already seen in uninjected specimens. Their only use, therefore, is to make more easy of demonstration that which was perfectly recognized without them.

It is singular to find that in infants and young children the intima of the arteries of the heart is sometimes thicker than the accepted histological standards teach to be normal, and of different structure. As I have so many times said, it is unusual to find the intima in arteries obtained post mortem to consist of a single layer of endothelium. It is much more apt to be formed of a cellular tissue of quite considerable thickness, and to be irregularly thick at different parts of the circle formed by the vessel. From what is known of embryology, it is almost certain that this condition of the intima does not exist during the earliest periods of development. How soon it comes on and whether it is only a post-natal condition are important questions ; but a much more important one is this—to what extent must the intima become thick or irregularly thick before the condition is to be looked upon as a disease injurious to the well-being of the individual and be named endarteritis or, if it be of a vein, endophlebitis ? Thickening of the intima of the arteries is in my opinion more common in the heart and in the kidneys than in any of the other organs.

In conclusion, it may be said, without much fear that the statement will be thought to be exaggerated, that the study of the blood-vessels of the heart has been a very fruitful one, more so perhaps than that of any other part of the body.

CHAPTER IX

The Blood-Vessels of the Lungs

It would probably be asserted by most anatomists and pathologists that the ramifications of the blood-vessels of the lungs are known to their most minute details, and that very little remains to be learned of the pulmonary circulation. Such an assertion would be entirely correct as far as concerns the larger blood-vessels, and most of the anatomy of the lung is unquestionably well known. I feel some doubt, however, in regard to the completeness of our knowledge of the minute structure of the lungs and of their blood-vessels. The large blood-vessels, the air-tubes, the connective tissue, and the spongy lung tissue are bound together in such a way as to form a very complicated whole. The lung structure is a more complicated one than that of the heart, for example, which is composed simply of connective tissue, muscle fibres, and blood-vessels. The larger blood-vessels of the heart are arranged according to a very simple plan upon the surface and in the substance, and the capillaries wind among and through the fibres. The microscopical details of the appearances of the larger blood-vessels of the lungs have not been worked out and recorded, as it is to be hoped they some day will be. It has been impossible for me to obtain a series of normal human lung blood-vessels of which I could have drawings made. My discussion will have to be confined, therefore, almost entirely to the elucidation of the subject of disease of the blood-vessels of the lungs. It is impossible, however, to study disease for any length of time without learning much of the normal conditions of the various tissues and organs that fall under observation. It may be hoped, therefore, in the course of my study of human lung blood-vessels, even if most of them are certainly diseased, and the normal condition of others is doubtful, that something will be acquired to add to the sum of knowledge of anatomy.

Fig. 76 is an illustration of a bronchiole surrounded by lung-tissue of a negro woman twenty-three years old who died of phthisis. When the autopsy was made, the pulmonary artery was injected with a solution of Berlin blue, and afterwards the tissue was stained in

FIG. 76.—BRONCHIOLE OF INJECTED LUNG. (× 115.)

From a negro woman twenty-three years old who died of phthisis. The tissue is stained red and the injected blood-vessels are blue. There is a fringe of capillaries that forms the greater part of the lining of the bronchiole, and outside of this are the submucous and the muscular tissues. There is no sign of the layer of columnar epithelium which ordinarily is one of the most conspicuous features of the bronchi and bronchioles in microscopical preparations.

Fig. 76.

bulk with borax-carmine and embedded in paraffin. The blue shows blood-vessels filled by the injection, and the red represents lung tissue and the bronchiole. A most curious development of capillaries is shown. In the natural condition the nutrient blood-vessels of the bronchioles are distributed in the outer layers like the vasa vasorum of the arteries and veins, but they do not penetrate very deeply into the substance of the bronchioles. The drawing shows that the capillaries pass entirely through the wall and are distributed, as seen in the section, in the form of a fringe upon the inner surface of the air tube. The folded and twisted appearance of the capillaries forming the lining of the bronchiole is probably due, principally if not entirely, to shrinkage of the tissue, just as the folding of the plicated membrane of blood-vessels is caused. This is an effect produced by the preparation of tissues for microscopical examination, which has already been described (page 9). In this bronchiole there are none of the columnar epithelial cells which in the natural condition form the lining of the minute air-tubes, nor are there any cuboidal cells such as are usually described as lying next to the layer of columnar cells. The whole character of the mucous lining of the tube is altered by the disease. Inside the layer of muscle the tissue is composed of round cells and capillaries; it is a granulation tissue and it is probably a good deal thicker than the natural mucous layer was. I do not know of any description or picture of this condition, although, of course, the increased vascularity of the mucous layer of inflamed bronchial tubes is well known. It is easy to understand why the expectoration so often becomes blood-stained, and even why quite copious hemorrhages take place in cases of bronchitis, and of pneumonia, and of phthisis, in all of which the bronchioles are inflamed, if it is a common effect of such inflammation to cause the development of capillaries to form the lining of the air-tubes. Every one knows how apt the nose is to bleed at certain stages of attacks of coryza, and this is due to the increased vascularity of the mucous lining. The changes of the mucosa of the nose are probably precisely similar to those shown by the drawing, and it is likely that the various stages of this process are similar to those that take place in the intestine in typhoid fever. At first probably the inflammation causes swelling and thickening of the lining of the bronchial tubes, then the mucous membrane, including the cuboidal cells and ciliated columnar epithelium, is shed. Later

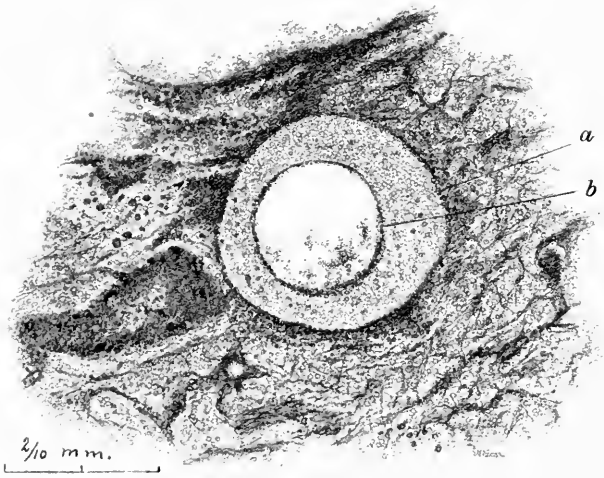
the granulation tissue, with its abundant supply of capillaries, is produced as a part of nature's attempt at regeneration ; this layer may be of even greater thickness than the natural mucous membrane, as it appears to be in the bronchiole shown by the drawing. The conditions demonstrated by this injected specimen are very interesting and suggestive.

Fig. 77 shows lung-tissue of a man seventy years old who died of chronic myelitis. There is a central space which appears to be empty except for a few blood-corpuscles scattered in it. Around this is a ring of closely appressed blood-corpuscles, outside of which is lung-tissue, all of which is infiltrated with blood. The lung-tissue is almost indistinguishable, for it looks like a mass of blood-corpuscles with lines and strings in it and some large cells and pigment granules scattered through. By itself, and without the knowledge that the tissue is lung, it is unlikely that it could be recognized. The escape of the blood from the capillaries of the lungs into the air-sacs is the cause of death in the great majority of people who die from natural causes. Laennec said that the brain, the heart, and the lungs are the three-legged stool (*trépied*) of life, and that death occurs much more frequently from cessation of the function of the lungs than from stoppage of the action of the brain or of the heart. The illustration, therefore, represents an exceedingly common condition, and one of great importance. When it is learned what happens toward the end of life to cause the capillaries to fail any longer to perform their work of containing and conveying the blood and it transudes into the air-spaces until life can no longer be maintained, a great advance in physiology and in pathology will result. The lung represented by Fig. 77 is that of an old man who had extensive fibroid disease of several of his organs, and it is probable that the space in the lung which is partly filled by blood is an emphysematous cavity. The exact effects of emphysema upon the blood-vessels are not yet completely known, but it is beyond question that it reduces the vascularity of any portion of lung that has become emphysematous. The number of the air-sacs is reduced by the breaking of many of them into one, and this must reduce the total area of their wall surface which is the carrier of the capillaries that oxygenate the blood. In addition to this, it is almost certain that the walls of the enlarged emphysematous vesicles are less richly supplied with capillaries than the

FIG. 77.—INFILTRATION OF THE LUNG WITH BLOOD. (× 100.)

From a man of seventy years who died of chronic myelitis. The lung-tissue is filled with infiltrated blood-corpuscles. *a* is the edge of an emphysematous cavity. The portion of this cavity between *a* and *b* is filled with blood-corpuscles which were pressed into it from the surrounding lung-tissue. In the centre the space is nearly empty,—it contains a few blood-corpuscles. The lung-tissue is distinguishable merely as lines and strings running through the mass of exuded blood-corpuscles. To the left there is a good deal of pigment. Such blood-exudation into the lung generally occurs during the last few hours of life. Only those who die suddenly escape it.

FIG. 77.



natural ones. It is highly probable, although at present impossible to prove, that emphysema is in part due to the fact that the increase of fibrous tissue, which is an essential part of the process, thickens and hardens the walls of the air-sacs, reduces their vascularity, and lowers their vitality, so that many air-vesicles become one by the breaking of their intervening walls. It has long seemed to me that under certain circumstances emphysema, which is a condition of disease, may be conservative of life. The number of the air-vescicles is beyond question reduced and their size is increased. They become so large that after death they may often be seen with the unaided eye standing out upon the surface of the lung as membranous blebs. If it is a fact that the walls of emphysematous air-sacs are less richly supplied with capillaries, it almost necessarily follows that the diseased lung made up of larger air-spaces which are less vascular will not be so prone to fill with blood. The old man of seventy whose lung is represented by Fig. 77 died of chronic myelitis, but it was discovered after his death that he had extensive fibrosis of the kidneys and of other organs. His death, which came after a very prolonged illness, was caused by filling up of the lungs; it was gradual in its approach, unlike those cases where death occurs suddenly by cessation of function of the brain or of the heart. It seems to me almost certain that if the lung had been less fibroid and less emphysematous—the air-cavities therefore smaller and the supply of blood larger—the transudation of the blood into the lung would have occurred sooner and more rapidly, and death would not have been so long delayed. The illustration shows that even after death the cavity seen in the centre of the drawing had only partly filled with blood, while the surrounding air-vescicles are entirely filled by the corpuscles which had escaped from the capillaries.

Figs. 78, 79, and 80, and Figs. 81, 82, and 83 together constitute a group of illustrations which show a curious result of disease upon the lungs and upon their blood-vessels. Figs. 78, 79, and 80 are drawn with low amplification, and Figs. 81, 82, and 83 give representations of portions of the same lungs more highly magnified,—showing something of the details of structure. Fig. 78 depicts lung of a woman twenty-three years old who died of typhoid fever. The lung appears nearly solid and the tissue is ill defined. Careful study of the section with higher amplification makes it certain that there is a

good deal of partially disintegrated blood. Fig. 79 shows lung of a negro woman twenty-eight years old who died of catarrhal pneumonia. It is by no means solid, but on the other hand the lung is of a much less open and spongy texture than is natural. There are open air-sacs alternated with patches that are more or less solid. When examined with higher amplification this lung shows no evidence of disintegration ; the tissue is clearly definable, and the walls of the air-sacs, the capillaries, and the blood-corpuscles within them, are in many places easy to distinguish, although in other and more solid portions the appearance is much like that of Fig. 78. Fig. 80 shows lung of a negro man forty-nine years old who died of Bright's disease. Far from presenting an appearance of solidity, the lung is of more open texture than is natural. Examination with greater amplification shows the tissue to be sharply defined. In the walls of the air-sacs the turns of the capillaries are easy to see, and so are the blood-corpuscles that in many places lie within them. These three drawings, when considered together, illustrate curious effects of acute and chronic diseases and the effects of disease at different ages upon the lungs. Fig. 78 is from a young adult who died of typhoid fever, which is a purely acute disease, and the tissue appears nearly solid. Fig. 79 is also from a young adult, but death was owing to catarrhal pneumonia—a disease only semi-acute in character—and the tissue, although denser than normal, is by no means solid. Fig. 80 is from a man past middle life who died of a chronic disease, and the tissue, far from being solid, is even more spongy and of open-meshed character than is natural. These microscopical appearances correspond exactly with the gross appearances of the lungs often found at post-mortem examination. In typhoid fever the exudation is frequently so great that the natural sponginess of the lung is destroyed, and it is in appearance nearly solid. In catarrhal pneumonia the sponginess is reduced, but the tissue is likely to look less solid ; while in Bright's disease (if it was of chronic character) the lung is often emphysematous and is even more spongy than normal lung is. In purely acute disease, the lung is apt to become and easily can become solid. In less acute or semi-chronic disease, this tendency is much less ; while in chronic disease, when there has been antecedent or accompanying degeneration, the lung remains open and spongy, the fibrosis seeming, as has already been said, to have an effect which may be conservative of

FIG. 78.—LUNG. (× 20.)

From a woman twenty-three years old who died of typhoid fever. The lung appears nearly solid, for most of the air-spaces are filled. *a*, the region shown more highly magnified by Fig. 81. Compare with Figs. 79 and 80.

FIG. 79.—LUNG. (× 20.)

From a negro woman twenty-eight years old who died of catarrhal pneumonia. The lung is much more nearly solid than natural, but many of the air-sacs are visible as empty spaces. *b*, the region shown more highly magnified by Fig. 82.

Fig. 78.

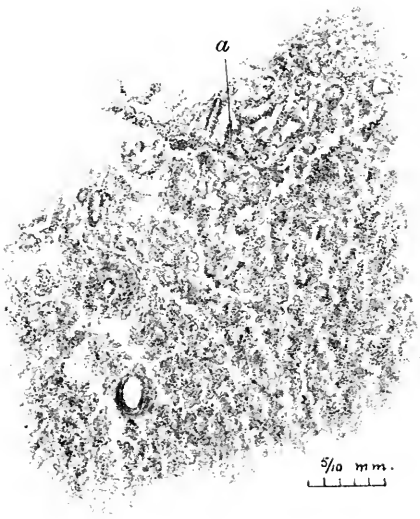


Fig. 79.

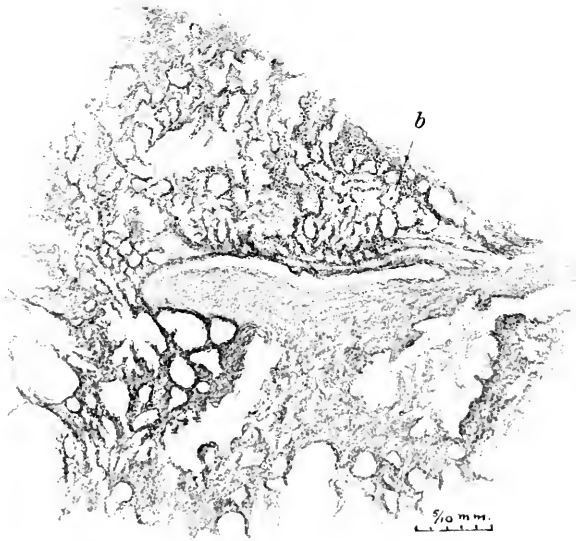
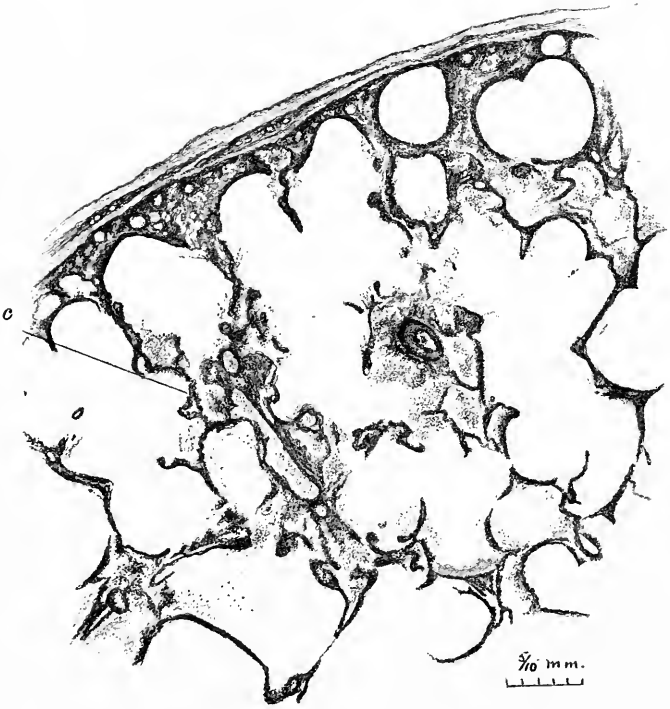


FIG. 80.—LUNG. (× 20.)

From a negro man forty-nine years old who died of Bright's disease. The tissue is of more open-meshed appearance than is natural, for there is emphysema of the lung. *c*, the region shown more highly magnified by Fig. 83.

FIG. 80.



life. This is because it is more difficult for transudation of blood into the air-sacs to occur, and therefore less easy for one of the legs of what Laennec has called the three-legged stool of life (the brain, the heart, and the lungs) to become unable to sustain its portion of the burden. The questions whether the blood-vessels undergo any structural alteration in such conditions of disease as those shown by Figs. 78, 79, and 80, and, if there is any alteration of structure, whether it is antecedent or subsequent, or if it is causative or resultant, are very important ones. There is no doubt that in cases of chronic disease of almost all kinds the larger blood-vessels are more or less abnormal in the majority of instances, and that they change with the progress of life, being found to be further and further away from the standards of the normal as men grow older. It is, however, much more difficult to be certain whether the changes of the larger blood-vessels—which are inevitable to advancing age and common in chronic disease at all periods of life, and are often found even in the very young—are causes of disease or are its consequences. This subject has been discussed in various parts of my book on the "Origin of Disease" and, in fact, it is the theme upon which much of it is built; I will not therefore pursue its discussion any further now. The condition of the capillaries, and the questions whether they become diseased and if their physical state can have any influence in the production of disease, are difficult ones, and the subject is one in regard to which much remains to be learned. If I am right in my previously expressed belief (page 17) that the capillaries are evanescent and come and go in the tissues as they are needed, it is unlikely that the subject of disease of capillaries ever will be formulated in the same way as that of disease of the larger blood-vessels is likely to be.

Figs. 81, 82, and 83 represent more highly magnified the regions *a*, *b*, and *c* of Figs. 78, 79, and 80. The greatest care was exercised by the artist to approach as nearly as possible to a reproduction of the appearances of the tissues themselves, and I am convinced, by what I have seen in the course of the examination of a great many capillaries and by what is shown by these drawings, that in disease there is often a real physical alteration of the capillaries themselves. A prolonged study of the capillaries has brought me to this conviction, but it has been attained by seeing in one section a single capillary, and in another a minute bit of tissue, and in a third

something else that tended to the same end. Much of the evidence, therefore, upon which my conviction is founded is of such a nature that it can only be told and nothing brought forward to demonstrate it by pictures. It has been exceedingly difficult to obtain tissues that show enough of the changes in the minute areas that can be included in single fields examined under high power with the microscope,—and it must be remembered that capillaries cannot be seen at all unless they are quite highly magnified. In drawing any conclusions in regard to disease of the capillaries from such preparations as those represented by the illustrations, it should always be kept in mind that it is almost certain that the capillaries in the living human tissues are branching tubes which run a reasonably direct course, and that they probably closely resemble those which may so easily be seen in the tail of the living tadpole. The convolutions and tortuosities of the capillaries represented by Figs. 82 and 83, which make them look like masses of earthworms as they intertwine themselves when many of them are put together, are produced to a great extent by the shrinkage of the tissue in the course of its preparation in various reagents before it is cut in sections for examination with the microscope. The resulting appearance is similar to the folding of the plicated membrane of the arterioles, which in living tissues is straight, as already described (page 12). Fig. 81 shows a portion of the walls of air-sacs and a bit of exudative substance which lay loosely in an air-vesicle. The tissue is ill-defined in appearance: there are cells of the lung, and the remains of blood-corpuscles which are partly disintegrated can be seen as imperfectly formed circles, but no capillaries can be distinguished. When considerable portions of sections of this lung are examined, it is easy to determine that there was extensive exudation of blood, and Fig. 78 shows that the lung was nearly solid. The patient, who was young, died of an acute attack of typhoid fever and probably had no antecedent chronic or latent disease: the capillaries had not undergone any physical alteration, and the cause of the transudation of blood into the lung-tissue and into the air-sacs under such circumstances is at present beyond the reach of explanation. Fig. 82 is also a portion of the walls of air-sacs, and there are a few scattered exudate cells. The lung-tissue contains many cells and the capillaries, which are tortuous, are easily distinguished. In places the circular blood-corpuscles can be seen, but more commonly the blood

has lost its distinctive appearance. This lung, which is also represented by Fig. 79, was in places nearly solid and in others quite open meshed. The patient, although a young adult, died of a subacute disease. It is fair to conclude that the capillaries are normal, or if at all abnormal that they are only a little thickened. Fig. 83 is also a portion of the lung showing the walls of air-sacs. The appearance of this portion of the lung presents a striking contrast to that of the two others just described. The walls of the air-sacs are from two to four times thicker and the tissue is of a much denser and coarser texture, which gives to it an appearance of heaviness. There are a great many capillaries which are very tortuous and there is not the slightest difficulty in seeing them. Many of the capillaries contain blood-corpuscles which are not disintegrated, but preserve their distinctive appearance. It is to be remembered that this lung, which is represented less highly magnified by Fig. 80, was even more open meshed in appearance than normal lung. The patient, who was past middle life, died of a chronic disease, and probably there was slowly progressive and increasing fibroid disease of his tissues and organs. The contrast presented by the three drawings, Figs. 78, 79, and 80, and Figs. 81, 82, and 83, is very striking and instructive. Fig. 78, a low-power picture, is the most solid of the three, while Fig 81, which is the same lung under greater amplification, appears least solid of the second three drawings. Fig. 79 is less solid, occupying in this respect a middle place, while Fig. 82 is of less light texture, more solid perhaps it may be said than Fig. 81, of the second three. Fig. 80 is the least solid of the three, or more correctly it is not solid at all, but is unnaturally open meshed and of a light texture. Fig. 83, on the other hand, is the most solid looking of the three drawings made with higher amplification. Thus it is seen that the one of the three lungs which when examined but little magnified is the most solid, appears on the other hand of the lightest texture when highly magnified, while that which when examined with low amplification is seen to be open meshed appears to be the most solid when it is highly magnified. The middle position of solidity is naturally held by the second of the drawings of both of the groups. Figs. 81, 82 and 83 have confirmed me in the opinion that the capillaries undergo actual physical alteration in disease. This opinion, as has already been said, I have long held on account of what I have seen in the course of the examination of many

sections of various tissues in which capillaries could be distinguished; but it seems to me that Fig. 83 demonstrates disease of the capillaries. The physical change consists in an increase of the thickness of their walls. A great effort was made by the artist to represent correctly the appearance of the tissues, and it is easy to recognize that the walls of the capillaries of Fig. 83 are of much heavier texture than those of Fig. 82, which are natural, or, if they are diseased at all, it is but little.

It is quite impossible at present to know the significance of such disease of the capillaries, but the mere demonstration of its existence may be a matter of considerable importance. If my contention that the capillaries are evanescent, and come and go in the tissues as they are needed, is correct, it is probable that in lung-tissue like that represented by Fig. 83 they develop less readily because the tissue is fibrous and hard, and that the same fibrous density which diminishes their facility of development renders them less easily extinguishable. The density of the walls of the air-sacs probably makes more difficult the transudation of blood, which in the great majority of cases is the direct cause of death. This lends confirmation to the view that emphysema is sometimes conservative of life.

My illustrations (Figs. 81, 82, and 83) are etchings which were drawn with the camera lucida on steel directly from sections, and they are as accurate as pictures can be, for the method is the best of which I know, and the artist is very skilful and exercised the greatest care in making them. It would be difficult to exaggerate the importance of the lessons taught by these three drawings. There are several of these lessons. First, the different tissues are of different degrees of density. Second, the tissue disintegrates before death in persons who die quickly of acute diseases, while the definition of all the different elements of the tissue is clear and sharp in those who die slowly and of chronic disease, and such tissues are satisfactory ones to study with the microscope. Last, but most important of all, is the increased thickness of the walls of the capillaries and the general increase of the fibrous tissue in the walls of the air-sacs of the lungs, as demonstrated by Fig. 83. The effects of emphysema and fibrosis, which are inevitable accompaniments of age, and often occur in the young who are prematurely old, is a subject of the highest importance, and the question how much influence the growth of fibrous tissue has in the production of the physical appearances commonly called

FIG. 81.—LUNG. (× 260.)

The region *a* from Fig. 78 more highly magnified. There is a portion of the walls of air-sacs and a little exudative material below. The capillaries of the lung cannot be seen.

FIG. 82.—LUNG. (× 260.)

The region *b* from Fig. 79 more highly magnified. The walls of air-sacs and scattered exudative material. The capillaries can be distinctly seen, and blood-corpuscles in some of them.

FIG. 83.—FIBROID LUNG. (× 260.)

The region *c* from Fig. 80 more highly magnified. The walls of the air-sacs are thick and the capillaries are easily seen. Many of them are filled with blood-corpuscles and the capillary walls are thicker than is normal.

Fig. 81

Fig. 82

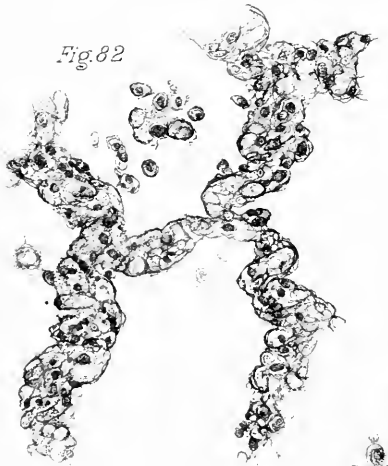


Fig. 83

5/100 m m.

those of age in human beings, and how much all of this may be counterfeited in younger persons by disease or by the effects of bad habits and unhygienic living, is of fascinating interest. My book upon the "Origin of Disease" is, to a great extent, made up by the discussion of these and allied questions, and it is therefore unnecessary now to enlarge upon them further than to say once more that it is important that the changes induced by fibrosis should be studied from every possible stand-point, so that the most minute changes that can be recognized by the use of the microscope may become well known. Thickening of the walls of the capillaries, such as that shown by Fig. 83, is probably one of the early changes, and it is very much to be desired that in time it may be learned whether it has any causative influence in producing fibrosis, or if it is solely a consequence. It is certainly true that much disease—probably most of the chronic disease —is of intrinsic origin, and has nothing to do with extrinsic poisons either of a material or of other nature. If such be the case, it is most likely that the blood-vessel system—which goes to all parts of the body and connects every part with every other part—is early affected in the course of chronic disease, and that the blood-vessels have a causative relation to the spread of the disease from their own walls and contained fluid to other tissues and organs. I do not wish to exaggerate the importance of the intrinsic origin of disease at the expense of truth, but at the present time there is so much exaggeration and so much misstatement in regard to the causation of disease by micro-organisms, that it becomes almost necessary to overstate the opposite position in order to offset the ill that is done by erroneous views now prevailing.

Figs. 84 and 85 show fibroid disease of blood-vessels of the lung. They are both from a negro infant one year old who died of chronic catarrhal pneumonia. He had whooping-cough when six months old, which ran into catarrhal pneumonia, and it soon became chronic, and from this disease he never recovered. The cough did not at any time cease, although there were periods of improvement when it was hoped he would get well. At times it was thought the disease was tuberculosis. As this infant was ill for six months and was only one year old when he died, he was continuously diseased during half of his life, which certainly justifies the statement that the attack was chronic. At the post-mortem, the examination with the unaided eye

failed to bring to light any evidence of disease of the lungs, the tissue of which appeared light and spongy. After portions of it had been properly prepared, a number of sections were taken from various regions and were cut. These sections show at once, and even before they are studied with the microscope, that the lung is greatly diseased. Most of the tissue is of open-meshed character and is quite normal, but scattered through this normal tissue are minute spots which are much denser. Examination with the microscope shows, even when low amplification is used, that the denser areas almost all include within them bronchioles and blood-vessels. Careful study shows that evidence of the existence of tuberculosis is entirely wanting. The case therefore is a typical one of broncho-pneumonia. It is believed by many that that disease has its origin in bronchitis and that the inflammation spreads from the bronchi to the surrounding tissue, thus producing peribronchitis, which must at the same time cause perivascular disease, because the blood-vessels and bronchi generally lie together, and it would therefore be impossible for the diseased tissue to surround the bronchi without including also many blood-vessels.

Fig. 84 is almost certainly an arteriole and not a vein, for veins do not have such a distinct plicated membrane. The intima, the plicated membrane, and the muscularis might almost be selected as types of what it is most common to find post mortem in human beings dead of disease. They are not typically normal, but, on the other hand, there is no evidence of very extensive disease, or of any disease that need have prevented the vessel performing its function. The intima is moderately thickened, for it is a cellular ring of quite considerable diameter, instead of being formed of a single layer of endothelial plates, as the histologists teach is normal in such minute arterioles as this. The plicated membrane is strikingly distinct and the muscularis is not of exactly even thickness, being a little thicker at some of its parts than at others. Outside the muscularis there is a ring of fibrous tissue of great thickness. The presence of a fibrous ring like this around an arteriole raises again the question which has already been discussed (Fig. 33), whether it should be classed as the thickened adventitia of the vessel or if it is perivascular connective tissue. There is nothing in the nature or in the appearance of this or of any other fibrous tissue which surrounds blood-

FIG. 84.—PERIVASCULAR FIBROSIS OF LUNG. (× 50.)

From a negro infant one year old who died of chronic catarrhal pneumonia. The striking feature exhibited by the arteriole is the thickening of fibrous tissue which surrounds the muscular coat. How much of this should be classified as adventitia, and therefore as an integral part of the vessel, and how much is perivascular connective tissue, it is impossible to determine. It is certain that so much connective tissue around a small arteriole of an infant is not natural.

FIG. 85.—PERIVASCULAR AND PERIBRONCHIAL PNEUMONIA. (× 20.)

From the same patient as Fig. 84. A blood-vessel with two bronchioles above it, in lung-tissue. The blood-vessel is probably an arteriole, but of this it is not possible to be certain because of the changes caused by disease. The blood-vessel and bronchioles are surrounded with dense tissue. The perivascular and peribronchial tissue is composed principally of round inflammation cells and contains many new blood-vessels, some of which can be seen even with the low amplification which was used in drawing the picture.

FIG. 84.

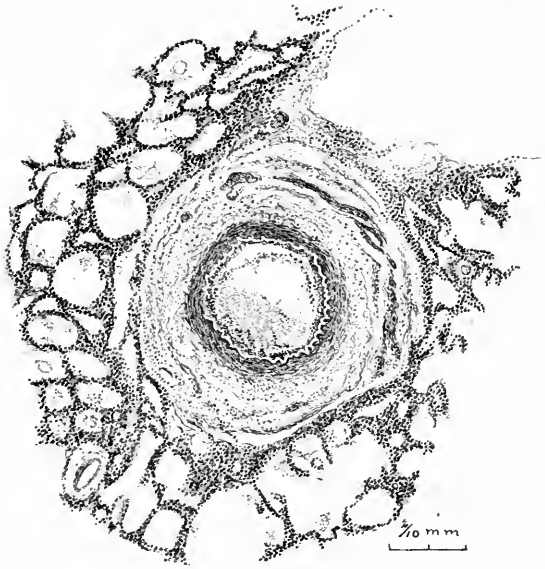
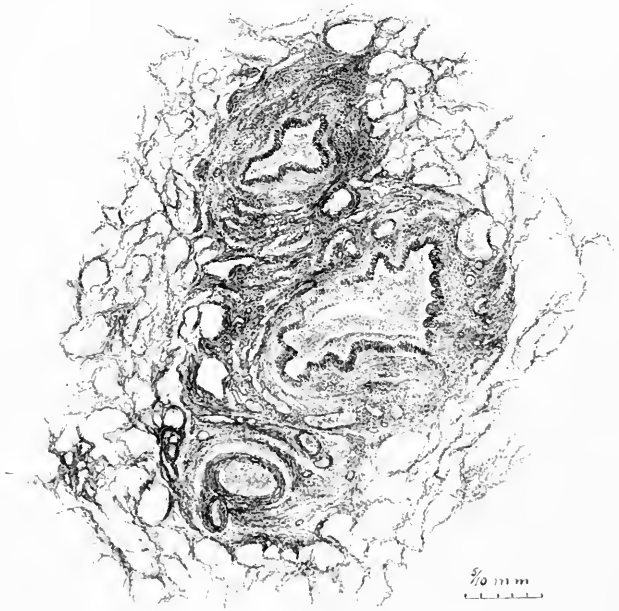


FIG. 85



vessels to make it possible to draw a distinction between adventitia and perivascular connective tissue. This uncertainty is of course entirely unimportant as far as concerns the possibility of understanding the disease, for the question is one purely of nomenclature. The great mass of fibrous tissue surrounding this arteriole is surely morbid, and as in this instance the arteriole stands by itself, there being no bronchiole very near, it affords evidence which seems to negative the theory that broncho-pneumonia results only from an extension of inflammation of the bronchi to the surrounding tissues. The appearance presented makes one think of the classical essays of Gull and Sutton and of their descriptions of what they have named arterio-capillary fibrosis. This disease they believed to have its origin in the adventitia of the blood-vessels and to be a prolific cause of chronic disease. All questions of the origin of disease are very difficult, and as far as regards real knowledge of final causes it may truthfully be said that it has not as yet been attained. Fig. 84 demonstrates a form of fibroid disease of the lung, and in the special instance the fibrosis is around an arteriole ; but whether the disease is truly of vascular origin or if it is due to some other cause is not now known. The growth of morbid fibroid tissue around the arterioles is a much less common form of disease than thickening of them from within owing to disease of the intima.

Fig. 85 is an illustration of lung-tissue from the same infant as Fig. 84. There are two bronchioles and a blood-vessel which is probably an arteriole. The three tubes are surrounded by dense tissue which is composed principally of round cells, and it contains many new blood-vessels. Some of these can be seen even with the low power which was used, and they are shown by the drawing. Greater amplification is required to bring out details of structure and show how numerous the vessels are. When the section is examined more highly magnified it is seen that the minute vessels have the character that is common to new blood-vessels which grow in inflamed tissues ; they are formed entirely of fibrous tissue which is of greater or less thickness in accordance with their size. It is very unusual for vessels of this character to have three coats. The arteriole is filled with blood, but like Fig. 84 its intima and muscularis are little if at all diseased. The vessel is surrounded by thickened fibrous tissue. The two bronchioles, like the arteriole, are surrounded by rings of dense

tissue which also contain many new blood-vessels. These are distinctly indicated by the drawing, although, as has been said, the amplification used was low. The lumina of the two air-tubes are partially filled by some material which is probably disintegrated mucus that would have been discharged as expectoration had life been sufficiently prolonged. The mucous lining of the bronchi is distinctly visible, and it may be that it is a little thickened or the cells proliferated owing to the bronchial inflammation which existed. The disease exhibited by the drawing is an increase of fibrous tissue around the bronchi and around the arteriole, and it is exactly similar to and a part of the same disease as that shown by Fig. 84. This curious morbid fibrosis occurred in an infant one year old who was ill with chronic disease during half of his brief life. Fibrosis of this character is in many respects similar to that which inevitably occurs in the aged, but which in some individuals begins much earlier than in others. Whether its primary seat and its cause lie in the blood-vessels or elsewhere is a question which remains for the future to answer.

Fig. 86 is an illustration of a vein of a man forty years old who died of an attack that was called typhoid fever. The clinical history and the post-mortem examination, however, when they are considered together, make the correctness of the diagnosis somewhat doubtful; but whether it is correct or incorrect, it is reasonably certain that the man had suffered from a malady which caused some chronic fibrosis of his organs prior to the fatal attack. The blood-vessel shown by Fig. 86 is called a vein because its inner coat and the muscularis look so much more like those of veins than of arteries. The intima is not well defined, and the muscular tissue is of open texture, as it has been shown (Fig. 13) that the muscularis of veins is,—a condition quite different from that of the muscularis of arteries, which has an appearance of greater density. The striking feature of the blood-vessel is the thick ring of fibrous tissue by which it is surrounded. The disease is somewhat similar to that shown by Figs. 84 and 85. This form of disease of blood-vessels is much less common than thickening of the intima.

Fig. 87 illustrates a portion of the lung of a man sixty-four years old who died of rapid phthisis. The drawing includes a portion of the pleura, and there are numerous blood-vessels of the character which it is common to find in tissues that were inflamed and in which

FIG. 86.—FIBROID VEIN OF LUNG. (× 50.)

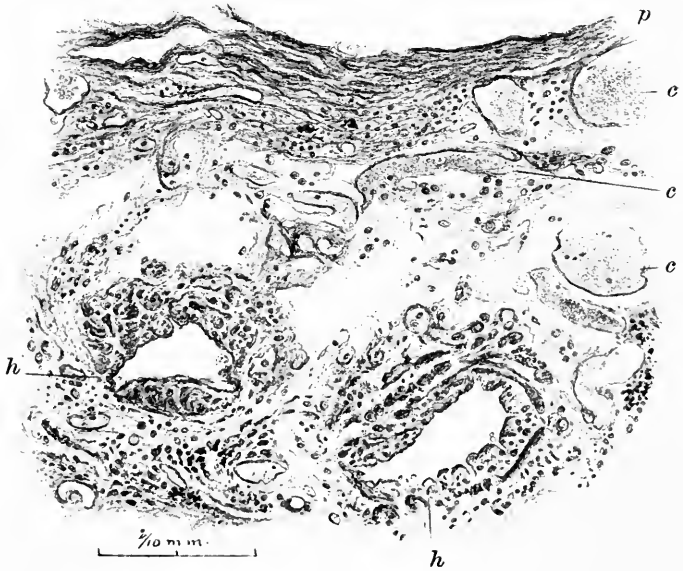
From a man forty years old who died of typhoid fever. *e*, epithelium of a bronchiole; *c*, cartilage; *b*, the vein. The true venous wall is thin, but it is surrounded by a thick ring of fibrous tissue. This is morbid and is due to perivascular disease having caused morbid fibroid deposit.

FIG. 87.—DISEASED BLOOD-VESSELS OF LUNG. (× 105.)

From a man sixty-four years old who died of rapid phthisis. *h*, *h*, the diseased blood-vessels; the walls are thickened and the tissue forming them hangs in festoons in the lumina. It is more like epithelium than like the ordinary tissue of blood-vessel walls. These vessels are like that shown by Fig. 72. *c*, *c*, *c*, capillaries, of which there are many more than the three indicated, for the tissue is very vascular. *p*, pleura, which is thickened and less distinctly defined from the lung-tissue below than is natural. Its deeper layers contain many capillaries.

FIG. 86.

FIG. 87.



fibrous tissue was growing, as it always does grow in the lungs of those who are suffering with phthisis unless it is of the most rapid character; and such was not the case in this instance, for it was one of the kind of cases in which the growth of blood-vessels is exuberant and in which the tissue of the lung becomes more dense. Some of the blood-vessels (*c*, *c*, *c*) are of good size and there are a great many of them, but those of this character are without three coats, their walls being composed entirely of fibrous tissue, and they are more or less thick according to their size. The walls of the largest blood-vessels of this class appear to be exactly like those of the smallest capillaries except for the difference of their thickness. Such vessels are probably of recent development, and they are common in inflamed tissues and in all sorts of growths, whether they be what are called new growths or hyperplasias. The important feature, however, of Fig. 87 is observed in the two blood-vessels *h*, *h*, and it is to show them that the drawing was made. They are probably veins, for the one of them to the right has shreds of muscular tissue scattered in the outer portion of its wall, which has the peculiar character of that shown by Fig. 34, and I have never seen the muscularis of an artery like it. The walls are thickened and the tissue hangs in festoons.

The appearance of the walls of these two veins is precisely similar to that shown by Fig. 72, which is from the heart. Such disease, and it is not at all rare, has at least two striking peculiarities of which I have not been able to find any published description. These are, first, that the tissue of which the thickened walls are principally composed is not like any normal tissue, and, second, that there are cells in it that present a peculiar appearance which I have never seen in normal tissue. This more nearly resembles epithelium than any other one of the normal tissues. The difference is not easy to describe, but is easy to recognize in properly prepared sections, and I think it is well shown by Figs. 87 and 72, as well as by others that I have published, especially by Figs. 21 to 27 in the "Origin of Disease." The peculiarity of the cells is that they are large and are generally composed of a central nucleus and a distinct external envelope with a space between which is filled by some sort of solid or fluid which did not stain. The appearance is very curious, and it is easily seen; there is a sharply defined external ring within which is an empty space except for the nucleus, that is generally situated in the centre, but is sometimes at one

side. In the preparation of Fig. 87 sufficient amplification was not used to show the peculiarities of the cells, but they are well shown by Figs. 21 and 22, "Origin of Disease," and they are described at page 52 of that work. In that case the blood-vessels described were almost certainly of recent development, for they were found in the anterior flap of the mitral valve of a youth fourteen years old who died of organic heart disease. In the natural condition there are few if any blood-vessels in the denser portions of the fibrous tissue of the mitral valve flaps.

The study of the blood-vessels of the lungs is somewhat unsatisfactory because it is inconclusive, and especially because at the present time it is impossible to obtain blood-vessels from which to make a set of illustrations to show an exact standard of normal adult human lung. It is to be hoped that the day is not distant when lung blood-vessels known to be normal will be obtained and drawings of them will be published. On the other hand, it cannot justly be said that this study has been without profit, for a number of curious and important questions connected with disease have been discussed and elucidated and something has been accomplished toward adding to the sum of knowledge of the anatomy of the blood-vessels of the lung. It may be not unprofitable, in conclusion, to review briefly the salient points that have been under consideration. The presence of capillaries in the lining of a bronchiole, so that they are entirely uncovered upon the inner surface of the tube, is shown by one illustration. This is a curious result of disease, and it must have important effects, and is probably of extremely common occurrence. I do not remember to have encountered any mention of this phase of disease in any publication.

The escape of blood from the capillaries of the lungs into the air-sacs is generally the last act of the drama of life, and it is a process which is as yet quite beyond the reach of comprehension. The illustration showing a pulmonary air-space which was probably enlarged by emphysema and is only partially filled with blood, but surrounded by lung-tissue overwhelmed by exuded blood-corpuscles, seems to indicate that emphysema may sometimes be conservative of life. For it must be that the walls of the air-sacs, if they become stiffer and denser under the influence of morbid fibrosis, are less prone to permit the escape of blood from the capillaries. If it be granted that my illustration (Fig. 83) and my statement that I have seen

other similarly thickened capillaries prove that the walls of the capillaries of the lungs become materially thicker in chronic disease, the observation is an important one, for I know of nothing as yet on record which demonstrates this disease so that it can easily be seen by every one. If the walls in the capillaries of lungs that have undergone morbid fibroid degeneration are thicker than normal, and the walls of the air-sacs are thicker, and if besides this my contention is correct that the capillaries are evanescent, and come and go in the tissues according to the need for them, then it must be that the number of them is less in fibroid lungs, for capillaries would certainly be less easily channelled out in dense fibroid tissue than in soft and elastic and open-meshed tissue.

The demonstration of perivascular and peribronchial fibrosis is curious and important, although it is impossible at present to say whether the disease should be classed as one of the blood-vessels or of the connective tissue; much less is it possible to say whether the lesion is causative of disease or is its consequence. The discovery by Gull and Sutton of the disease that they named arteriocapillary fibrosis marked an important advance of pathology, but it has always seemed to me that some of their reasons are inconclusive, and especially that their illustrations fail to show what was plain to them in their microscopical preparations. My illustrations of morbid fibroid tissue around arteries and veins, and of fibroid thickening of capillaries, are probably instances of the disease described by Gull and Sutton. Their demonstration of fibrosis of capillaries was very imperfect, if not a failure. It is astonishing, and highly creditable to their acumen as observers, that they should have been able to go so much further in their conclusions than their illustrations clearly demonstrated. It is generally the case that those who make microscopical investigations can satisfy themselves and are able to form opinions in regard to things they have seen which at first they are unable to demonstrate to others by pictures. It must be very rarely that a question of importance can be determined from a single microscopical preparation and an illustration made, but conclusions are reached which are correct by seeing a little at one time and a little at another.

The demonstration of the existence of very numerous new blood-vessels in phthisical lung is curious, but is no more than might be expected and that is well known to occur. Anything that causes

such rapid proliferation of cells and so great tissue growth as occurs at certain stages and in certain forms of phthisis must cause the formation of new blood-vessels. Endarteritis is a disease that has been very extensively studied of recent years, but comparatively little attention has been bestowed upon endophlebitis. A type of this latter disease is shown by Figs. 34 and 35. The effects of these curious changes of the lining of the arteries and veins are not yet known, but they must be important. The redundant growth of the intima shown by Fig. 87 is most singular, and it is very common. Morbid proliferation of the intima, called endarteritis, is the most common disease to which arteries are liable, and there is good reason to think that endophlebitis also is of much more frequent occurrence than has heretofore been supposed. The tissue which composes these morbid thickenings of the lining of blood-vessels is quite unlike any normal tissue, and I have not been able to find any adequate published description of it nor any explanation of its cause. The lungs I believe to be the most liable of all the human organs to disease.

CHAPTER X

The Blood-Vessels of the Liver

The liver is not of such simple structure as, for instance, the heart and kidney, and its anatomy is not so well known as it some day will be. Although the intimate connections of the capillaries with the columns of secreting cells, and the general course of the hepatic arteries and of the portal and hepatic veins and the bile-ducts are well known, it cannot be justly claimed that the exact relations of the capillaries to the columns of secreting cells are perfectly understood. Nor is it certain whether the blood ever comes directly in contact with the secreting cells of the liver without an intervening capillary wall in the way that it is thought by some of the most distinguished authorities that the blood bathes the cells in the pulp of the spleen. The fibrous framework that constitutes the skeleton of the liver and forms the support for the trabeculæ of secreting cells is quite strongly made. This may be seen in well-prepared sections of what is called "nutmeg liver,"—a subject that I discussed in my book on the "Origin of Disease," at page 102, and demonstrated by Figs. 71, 72, and 73, and others in that work. The density of the fibrous framework is well shown by Fig. 72, and the appearances there represented make it difficult to believe that the capillaries always have a distinct wall of their own to prevent the blood coming directly into contact with the secreting cells. That drawing seems to me to suggest that there is not always a separating capillary wall between the blood and the secreting cells. It must be remembered, however, that the illustration was made from diseased tissue, and it is impossible to be certain whether the normal conditions are ever similar to those there represented. My previously published description ("Origin of Disease") of this condition seems to me to be somewhat inadequate in several respects, and especially in this: that it does not sufficiently emphasize the fact that the ordinary anatomical descriptions do not make plain how strong and distinctive a structure is the fibrous framework which constitutes the skeleton of the liver. There can be little doubt that something still remains to be learned regarding the anatomy of the liver.

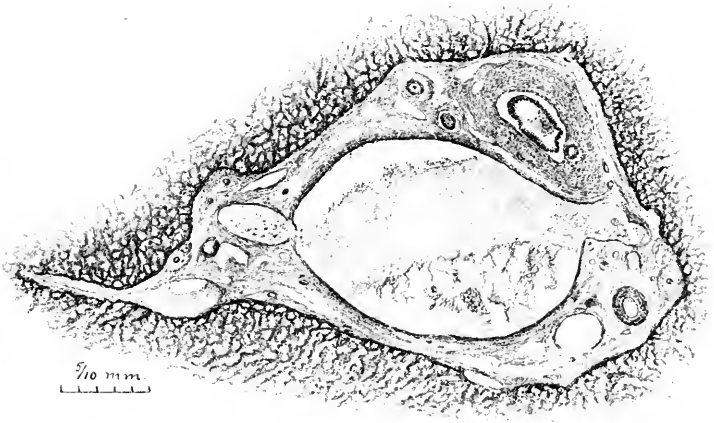
It has been impossible for me to obtain a set of normal blood-vessels of the liver from which to have drawings made, just as it was impossible to obtain such a set of blood-vessels from human lungs. A knowledge of the natural histological appearances of the blood-vessels of adult human liver cannot be obtained from the study of existing publications. So much of what is known has been learned from the examination of the tissues of the lower animals that it is often very difficult or impossible for any one studying the subject to know whether particular blood-vessels are diseased or healthy, because there is no accepted standard of the normal to which to turn to decide the question. It is very probable that through the continued study of the pathology of the liver a great deal may be learned of its anatomy, for even in pathological tissues some of the blood-vessels are not diseased.

Fig. 88 shows a section of a portal vein and surrounding vessels of the liver of a man twenty-three years old who died of empyema. The large portal vein which occupies the centre is partially filled by clot, and in the fibrous tissue with which it is surrounded there are bile-ducts and branches of the hepatic artery as well as other openings which are probably smaller branches of the portal vein. The group is such an one as it is most common to find in specimens of human liver that are obtained in the course of any routine series of post-mortem examinations. I am unable to recognize that these blood-vessels are diseased, and yet they are not at all like what the ordinary anatomical teachings would lead us to believe to be normal. The wall of the large portal vein is composed of nothing but fibrous tissue without the slightest approach to any division into three coats, and the walls of the branches of the hepatic artery are thick. This latter may be due to shrinkage in the course of preparation for section, or it may be that it is common for the minute arterioles in human adult tissues to be much thicker walled than ordinary anatomical descriptions teach. Something of what has been described can be seen in the drawing, but greater amplification is required to make it possible fully to recognize the details of structure. When more highly magnified the section distinctly shows what has been asserted regarding the blood-vessels. This drawing, which is of a kind that is very common to find, shows how it is often difficult to decide whether a tissue is diseased or normal, and at the same time it emphasizes my

FIG. 88.—CROSS-SECTION OF A PORTAL VEIN AND OF OTHER VESSELS IN THE CAPSULE OF GLISSON. (× 24.)

From a man of twenty-three who died of empyema. The portal vein, hepatic arteries, and bile-ducts are fairly representative of such vessels as they are found in adults. They are, however, quite different in appearance from the ordinary pictures in text-books of histology.

Fig. 88.



statement that it is very desirable that a standard of the normal of the hepatic blood-vessels should be obtained.

Fig. 89 depicts a group of vessels of the liver of a man sixty-two years old who died of hepatic cirrhosis. In the centre is a good-sized portal vein which is cut across. Above this, to the left, is a smaller portal vein which has very thick walls, and to the right, above the large portal vein, is a thick-walled hepatic artery. A striking feature of the disease is that in the walls both of the large portal vein and of the smaller thick-walled one there are many minute new-formed blood-vessels. Greater amplification brings out details of structure which are not shown by the drawing, but this exhibits the most important features. The new blood-vessels are very numerous in the thickened wall of the smaller portal vein, which is above and to the left, and they are of the nature of capillaries with thin walls of fibrous tissue, as it has already been shown that new vessels are when they are first developed and are still small. The thickening of the wall of the hepatic artery is mostly, if not entirely, due to unnatural growth of the intima, although it may be that the muscularis is slightly thickened. The wall of the large portal vein is probably somewhat thicker than normal and there are a good many vessels in it, some of which are almost certainly of new growth. Altogether the drawing shows a typical example of what might be expected to occur in cirrhosis of the liver, a disease of which the most important feature is the growth of fibrous tissue. There is much more fibrous tissue in the portal channel than is normal, and all of the blood-vessels except those of new growth, which were lately developed to nourish the increase of tissue, are thick walled. It is curious that the tissue composing the thickened portal vein is purely fibrous, there being no division into different coats, while the thickened hepatic artery has three distinct tunics and it is the intima which is thickened. Endarteritis of this form is the commonest of all known diseases of the blood-vessels, as has already so often been said, and it is singular that the diseased hepatic artery and portal vein which lie so close together, and are therefore by their contiguity exposed to the same influences, should both be thick walled, but that the nature of the thickening should be so entirely different. It is at present impossible to know whether this condition is due to a single cause which within a small area operated differently, and so as to produce different results upon the portal vein and the hepatic

artery, or if there were two separate causes of disease. Another strange and curious fact often observed in cases of disease of blood-vessels (which is shown by the drawing) is that where arteries or veins lie close together one may be greatly diseased while the other remains healthy, or even one portion of the same blood-vessel may be much diseased while another part close by is quite normal. The large portal vein in the centre of Fig. 89 is but little thickened, while the small one to the left and above it is so thick walled that its lumen is almost closed, and yet the two are in contact and the smaller is probably a branch of the larger one.

Fig. 90 shows a section of the anterior-inferior edge of the liver of a man sixty years old who died of dilatation of the heart. The knife-like sharpness of the edge of the liver, and the fluting of its margin, were easily distinguished with the unaided eye at the autopsy, and it is almost certain therefore that they had existed during life and were not the result of post-mortem shrinkage. The capsule is thickened and the greatest proportion of the liver included in the illustration is composed of fibrous tissue, although there is quite a good deal that is formed of the secreting cells. This is plainly shown by the drawing, but of course it is possible to make a much nicer distinction between the different kinds of tissue if the section is examined more highly magnified. The most striking feature of all, however, is the extreme and unnatural multiplicity of the blood-vessels. Most of these lie in the morbid fibrous tissue and are not surrounded by normal liver. It is impossible to be certain whether the vessels were newly developed or are the natural blood-vessels squeezed together by the condensation and shrinkage caused by the growth and contraction of the fibrous tissue. It is most probable that the original vessels are still present and have been pressed more nearly together than they were before the liver became diseased, but it is almost certain that some of the blood-vessels here are new. This opinion is supported by the facts that many of them have the appearance of new vessels and that the blood-vessels here are too numerous for it to be possible that they are nothing but the natural ones. The subject of the development of new blood-vessels in adult tissues is a very important one and it is discussed in Chapter III of this work and in Chapter IV of my book on the "Origin of Disease." Figs. 15, 18, 19, 20, and 21 in that work represent blood-vessels in various stages of growth and they are almost

FIG. 89.—THICKENING OF A PORTAL VEIN AND HEPATIC ARTERY. (× 24.)

From a man sixty-two years old who died of cirrhosis of the liver. A section of the liver. The large space is the calibre of a portal vein containing some blood. Above it to the left is the thick-walled portal vein, and in its walls are many new blood-vessels. To the right of this thick portal vein is an hepatic artery, which is also thick-walled. The intima especially is thickened.

FIG. 90.—ANTERIOR-INFERIOR EDGE OF A CIRRHOTIC LIVER AND BLOOD-VESSELS. (× 20.)

From a man of sixty years who died of dilatation of the heart. The puckering of the hepatic tissue and fluted appearance of its edge were easily seen with the naked eye when the post-mortem examination was made. The greatest part of the tissue is fibrous, but a good deal of liver-tissue still remains. The number of blood-vessels crowded in the space is very great, and it is impossible to ascertain how many of them are new vessels and how many are the natural vessels squeezed together by the shrinkage. Many of the blood-vessels are very thick-walled owing to disease, and there is one large one and other smaller ones of which the lumina are nearly closed.

FIG. 89.

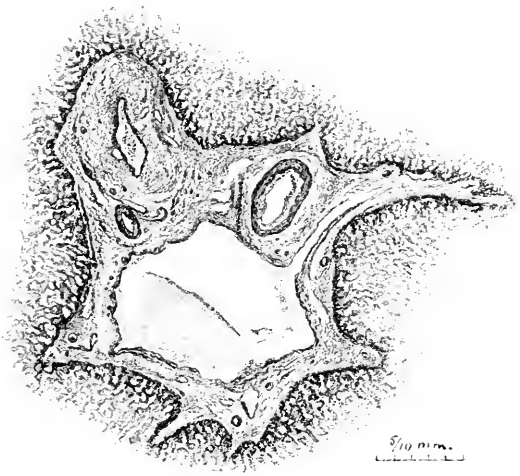
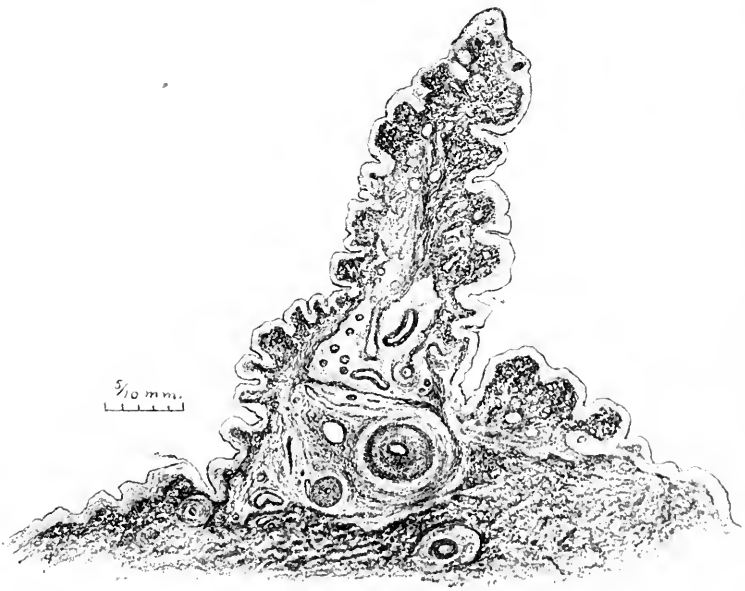


FIG. 90.



surely due to a new development of tissue. Fig. 15 is a pair of imperfect blood-vessels in the wall of an aneurism, and Fig. 21 is a vessel in the thickened and diseased anterior leaflet of the mitral valve. These are in many respects like the large thick-walled vessel with a very small lumen shown in the centre of the drawing Fig. 90, and of some of the other smaller ones which are scattered around it. The largest one when it is examined with greater amplification distinctly shows the plicated membrane. Whether this is a certain indication that it was a natural vessel which became thickened and nearly closed owing to disease, or if the vessel is purely a new development, it is impossible at present to ascertain. After having examined a great many such vessels in various kinds of tissues, my own conclusion is that it is often very difficult to decide when studying any particular one whether it is a new growth or if it is only one which was once normal and has become changed and distorted by disease. The drawing also shows other and thin-walled vessels, such as commonly develop in new and proliferating tissues. The details of this are easily seen if the section is examined with greater amplification.

Fig. 90, like Fig. 89, is beyond question a type of cirrhosis of the liver, although the case was classified clinically as one of death from dilatation of the heart. The combination of a greater or less degree of fibrosis of the liver with organic heart disease is so usual that it may in the majority of instances be expected to be present. A number of striking and peculiar lesions of cirrhosis are exhibited by the drawing. There is a very great amount of morbid fibrous tissue which has replaced a corresponding amount of liver substance. The number of blood-vessels that exist in so small a piece of liver is extraordinary, and most of them are in the morbid fibrous tissue and not in the natural tissue of the liver that remains. The blood-vessels are both of the thin-walled variety that are always found in new and proliferating tissues, and which are certainly of new development, and of the thick-walled nature which also are generally found in new and proliferating tissue but in regard to which it is impossible at present to decide whether they are of new development or are natural vessels changed and distorted by disease. The thickness of the fibrous capsule and the manner in which the whole of the surface of the liver that is shown in section is fluted are very striking, and more striking still perhaps is the sharp knife-like form which was assumed by the anterior-inferior

edge of the liver, which is distinctly shown by the drawing. It is to be recollected that these two features—the knife-like sharpness of the edge of the liver and the puckering of the surface—were easily distinguished with the unaided eye at the post-mortem examination, and that they had therefore almost certainly existed during life. They constitute a striking example of the effects produced by the tendency of morbid fibroid tissue constantly and progressively to shrink and to cause distortion. In conclusion, it may be not without advantage to repeat that the minute anatomy of the liver is still only imperfectly known, and that it is greatly to be hoped that the time may not be far distant when an exact knowledge will be obtained of the standard of what is normal in the blood-vessels of the human liver.

CHAPTER XI

The Blood-Vessels of the Spleen

There is less known of the anatomy and of the function of the spleen than of any other of the great organs. It is classified as belonging to the system of lymph-glands, and it is very probable that it has to do with the production or with the destruction of the blood-corpuscles, but neither of these things is certain. Nor is the anatomy of the spleen well understood. The organ consists of fibrous tissue, of lymph-cells, and of lymph- and blood-vessels. The fibrous tissue forms the capsule, which covers the entire surface of the organ; the trabeculæ, some of which are quite large and strong and of complicated structure; and the reticulum, which supports the lymph-cells. The fibrous tissue of the spleen contains many connective-tissue corpuscles and these cells are of an infinite variety of forms. As the connective-tissue cells of the spleen are of such varied appearance, and as the lymph-cells also are liable to differ greatly under differing circumstances, it can readily be understood that cells varying much in appearance are found in the spleen. The exact manner in which the lymph-cells are supported by the fibrous reticulum and their relations to each other are not understood in the same way, for instance, as the mutual relations of the epithelium and connective tissue of the kidney and those of the muscular and fibrous tissues of the heart are known. The experiment of treating spleen tissue with a reagent which will partially disintegrate it, and then washing it to remove the lymph-cells, has been made. The material that remains after such treatment can be seen with the microscope to consist of a fine fibrous reticulum in which the lymph-cells were supported. This test, however, although very interesting and instructive, is rather crude, and does not demonstrate anything that had not already been learned by the examination of sections and even by the older and still coarser methods of microscopical examination. It is in the highest degree improbable that the pulp of the spleen consists of a reticulum which is without orderly arrangement, in which the lymph-cells are irregularly distributed as a handful of seeds might be if they were thrown into a tangle

of loose hay. The splenic reticulum is almost certainly developed according to some simple system, and even in adult tissues it probably is still a well-organized structure, and it is equally probable that in this the lymph-cells are disposed in a manner which is as orderly as that of the columns of secreting cells of the liver or of the epithelium of the kidney. The very word "pulp," which is commonly employed to designate the tissue which composes the substance of the spleen, is significant of the present lack of understanding of the anatomy of the organ. Imagine an anatomist speaking of the tissues of the heart, liver, or kidney, which structurally are so beautiful, as pulp!

The lymph-vessels of the spleen are so little understood that it is not worth while here to try to describe them. The blood-vessels are the subject of the chapter, and much that is final regarding them is already known, but on the other hand a great deal remains still to be learned. There are capillaries in the spleen just as there are capillaries in most other tissues, and these can easily be seen in well-made preparations. It has, however, been very generally taught that the circulation of the spleen is different from that of other organs, in that the blood is not always confined within arteries, veins, and capillaries, but that under natural conditions in the pulp, both the corpuscles and the liquor sanguinis of the blood pass unconfined by any blood-vessel wall into the reticulum and among the lymph-cells. If it is natural for the blood of the spleen to come in direct contact with the lymph-cells, and for the corpuscles and liquor sanguinis to pass freely among and around them, it is necessary to conceive of a structure quite different from that of any of the other organs and tissues. Even to imagine such a structure is difficult, for its existence would necessitate the absence of connective tissue, and the absence of connective tissue from any one of the softer tissues, which is their only supporting framework, would involve chaos. It is absolutely impossible to believe that the spleen tissue in any part of the organ can be of such a nature as to form a pulp constituted of a mixture of lymph-cells, blood-corpuscles, and liquor sanguinis—just as good-sized pebbles, fine sand, and water might be mixed in a bowl. The circulation of the blood has been studied to its most minute details and its mysteries unravelled in the transparent tissues of some of the lower animals, and nothing has been seen to support

the view that the blood ever normally escapes from the restraint of the walls of the blood-vessels. The circulation when studied in the lower animals shows the blood flowing within the walls of the vessels, and it is only under the influence of morbid conditions—like irritation and inflammation—that it can be seen to escape into the tissues. It is not necessary to tell here at length how the blood-corpuscles flow slowly at the periphery and more rapidly in the middle of the stream in a capillary which lies within a portion of tissue that becomes inflamed, and how then the white cells squeeze out through the membranous wall of the capillary and lie free in the surrounding tissue. The instant effect, however, is disease, and tissue diseased in this way never rests until it has rid itself of the effused blood or is dead. It is difficult to believe that it can be normal for the blood to flow through the spleen without the membranous walls of the capillaries to restrain it and to guide its flow.

It might be thought that the study of injected specimens of adult human spleen would decide this question whether the blood flows in the organ unconfined by any blood-vessel wall, but I have made such preparations and have examined them carefully and they throw no light upon the subject. These preparations are described at page 21.

In the injected preparations of spleen which show the cells of the organ surrounded by blue nets, it is certain that the injection material fills spaces which surround the cells, and that these spaces look like a system of tubes; but it is impossible to ascertain whether the spaces have walls which separate the blue injection from the cells or if this lies directly in contact with them. I am thus driven back to the conclusion that, although it is a fact that the blue injection is forced into minute spaces around the cells, it is impossible at present to ascertain whether these are torn open in the tissue by the injecting force, and are therefore abnormal, or if they are natural tubes between the cells, and, if they are natural tubes, whether they have separate capillary walls of their own or are without walls. It is, then, true that experiments made of injecting the spleen do not throw any light upon the unsolved problems regarding the circulation of the blood in the capillaries of the organ. Much, therefore, still remains to be learned of the capillaries of the spleen and of the ultimate ramifications of the blood in the organ. It has been impossible for me to obtain a set of sections of arteries and veins of the spleen from which I could have drawings made to show

as types of the normal, just as I have been unable to obtain typically normal blood-vessels of the other organs. It is a peculiarity of the anatomy of the spleen that most of its larger arteries and veins lie in the trabeculæ, and are therefore surrounded and supported by fibrous tissue.

Fig. 91 depicts two arteries and a vein in a trabecula of the spleen of a boy eleven years old who died of acute peritonitis. Neither the vein, which is the central vessel, nor the arteries, which lie on either side of it, are like blood-vessels that are described as normal, and yet all three are fair types of what it is most common to find in such spleens as are obtained at post-mortem examinations. In this instance the patient died of a disease which affords no ground for the assumption that there had been latent vascular disease previous to the final fatal attack. The vein is a fibrous ring, and, although it has a somewhat differentiated wall (so that it cannot be said to be a simple channel hollowed out in the fibrous tissue of the trabecula), there is nothing like a division of the wall into three coats, as is said to be normal in veins of this size. The arteries, and especially the larger of the two, show some thickening of the muscular coat, and the intima instead of being a thin layer of endothelium is quite thick. The appearance is typical of what is most common in human spleen and in other tissues. These arteries are more thick walled than is normal, the intima being more affected than the other two coats. At the same time, the vein has not three defined coats, but is formed purely of fibrous tissue. A peculiar feature is that there are two arteries and only one vein, whereas it is a much more common thing in most tissues to find a single artery with two accompanying veins.

Fig. 92 shows the blood-vessels in a trabecula of the spleen of a man forty-eight years old who died of dysentery. The central vessel appears to be an artery and the two others to be veins. It is quite common to find such vessels in the spleen. The walls of the artery are fairly well defined, three coats being distinctly visible ; but the veins are merely openings in the fibrous trabecula, there being nothing like three coats and not even a trace of muscular tissue distinguishable. It is impossible to say whether the condition is due to disease, or if such a departure from the accepted standard of the normal can be due to the time of life, for the man was past middle life, although by no means sufficiently advanced in years to be classed as old. It

FIG. 91.—BLOOD-VESSELS OF THE SPLEEN. (× 50.)

From a boy of eleven years who died of acute peritonitis. Blood-vessels in a trabecula of the spleen. The large vessel in the middle is a vein, and to right and left of it are two arterioles. There is no reason to suppose that the child had suffered with disease of the blood-vessels, and yet neither the vein nor the arteries are like the accepted standards of the normal. The vein is a tube of fibrous tissue without distinct differentiation into three coats, while both the arterioles have thick muscular coats, and their intimas are thicker than is natural in such small vessels. It is common in pathological investigations to find the blood-vessels like these rather than like the pictures in text-books which are said to represent the normal.

FIG. 92.—THREE BLOOD-VESSELS IN A SPLEEN TRABECULA. (× 50.)

From a man of forty-eight years who died of dysentery. The central vessel is almost certainly an artery and the two others are veins. It is common to find vessels like the two veins in the spleen. They are almost without differentiated walls, being merely openings in the fibrous trabecula. Neither intima, nor muscularis, nor adventitia can be distinguished. It is impossible to say whether such a condition is the result of disease or if it is natural at forty-eight years of age.

FIG. 91.

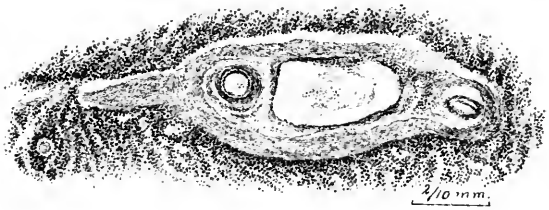


FIG. 92.

is unquestionably true that very considerable changes take place in the tissues as life advances. The two drawings, Figs. 91 and 92, present interesting points of similarity and of contrast. In Fig. 91 the walls of the arteries are distinctly thickened, and in Fig. 92 the wall of the artery is somewhat ragged, but presents no striking departure from the normal. In Fig. 91 the wall of the vein is not divided into three coats, and has no muscular tissue in it, but there is a fibrous wall, differentiated from the tissue of the trabecula in which it lies. In Fig. 92 the veins appear simply as openings in the trabecula, there not being anything like differentiated walls to serve as frames. It might be said that the peculiar appearance of the veins of Fig. 92 is due to faulty technique in preparing the section, that there were during life differentiated walls of the veins and that they were torn out or dropped out in the course of preparation of the tissue. This tissue, however, was prepared in a manner exactly similar to that used in preparing other sections, and I do not believe that anything was lost, but that the condition resulted from disease. Pathologists often explain conditions that are difficult to understand by saying that they resulted from bad technique, and by this evasion they fail to recognize important truths.

Fig. 93 is an illustration of an arteriole in a trabecula of the spleen of a man fifty-four years old who died of Bright's disease. This blood-vessel can be certainly recognized as an arteriole by the appearance of its muscular coat. The muscular coat is of compact structure and forms a thin layer of about even diameter around the vessel, and inside this lies the intima which is very greatly and unevenly thickened. I have never seen the muscular layer of a vein present an appearance exactly similar to this. It is therefore reasonably certain that the vessel is an arteriole. The disease that affects it is endarteritis of the form which has already been said, in connection with the descriptions of other organs and tissues, to be the commonest of all the diseases that attack the blood-vessels. In order to appreciate everything that is shown by this arteriole it is necessary to examine it with greater amplification, but most of the characteristics, and certainly the most important ones, are shown by the drawing. The intima is greatly and irregularly thickened. So irregular is this thickening that the opening of the vessel is unsymmetrically placed instead of being in the centre. If the section is examined more

magnified it can be seen that many of the cells which form the intima have the peculiar hollowed appearance that is described at page 103 as common in diseased intima, and which is quite unlike that of any normal cell or tissue. Outside the intima is the muscularis, which, it has already been said, forms an even circle of closely felted tissue. No distinction whatever can be made out between the adventitia of the arteriole and the fibrous tissue of the trabecula in which it is included. The spleen is an especially good organ in which to verify the correctness of the assertion made at page 6, that arteries and veins should be considered to have only two coats—the intima and muscularis—and that what is described as the adventitia should be regarded as a part of the perivascular connective tissue by which all blood-vessels are surrounded. It is always impossible to draw a line of distinction separating the perivascular connective tissue from the adventitia, and frequently in the spleen—and unusually well in this drawing of spleen—it can be seen that the fibrous tissue of the trabecula is an even and uniform structure abutting directly against the muscularis of the arteriole. Sometimes, as the conditions shown by this drawing prove, the adventitia and the perivascular connective tissue are absolutely indistinguishable, but more often sections of the spleen present the appearance of Fig. 91, which shows that the fibrous tissue immediately outside the muscularis of the arterioles is of looser texture than the rest of the trabecula. This trabecula (Fig. 93) contains a greater number of cells than is usual in the trabeculæ of the spleen, which, when examined in sections, often appear to be almost acellular. The morbid conditions that have been described are exactly what might have been expected *a priori* to exist in the spleen of a man of fifty-four who died of Bright's disease, for that malady is prone to cause fibrosis and inflammation and disease of the blood-vessels. The most striking thing which is shown by the drawing is the endarteritis, and it can hardly be said too often that endarteritis is the commonest disorder to which the blood-vessels are subject. It occurs at all ages and is found in the tissues of persons dead of every known disease, and yet its extensive existence in the body is not incompatible with the continuance of good health.

Fig. 94 shows thick-walled blood-vessels of the spleen of a man seventy years old who died of chronic myelitis, and who had contracted kidneys and general fibrosis of many organs. There are four blood-

FIG. 93.—THICKENED BLOOD-VESSEL IN SPLEEN. (× 50.)

From a man fifty-four years old who died of Bright's disease. The blood-vessel is probably an arteriole and it lies in a trabecula. Its walls are thickened and its opening is not in the centre owing to the irregularity of the thickening. There is a great increase of the number of cells in the trabecula owing to the disease.

FIG. 94.—FOUR THICKENED BLOOD-VESSELS OF THE SPLEEN. (× 50.)

From a man seventy years old who died of chronic myelitis. It is impossible to know whether such thickened and diseased vessels are arteries or veins; but they are more like arteries. They all lie in the fibrous trabeculæ. The two larger ones have thickened walls and the muscular tissue is still easily seen. The greater part of the wall is composed of the thickened intima. The two smaller ones are almost closed.

FIG. 93.

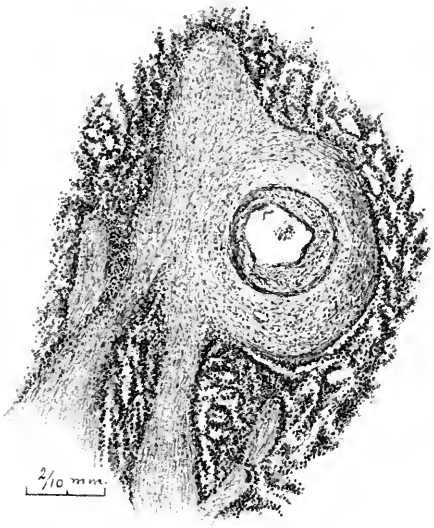


FIG. 94.

vessels, two larger and two smaller ones, all of which lie in the trabeculæ, and it is impossible to be certain whether they are arterioles or veins, but I believe them to be arterioles. These blood-vessels are affected by endarteritis. The two smaller ones are so thick-walled that their calibres are nearly obliterated. The larger ones, especially the upper of the two, furnish another striking example of disease exactly similar to that shown by Fig. 93. This upper arteriole exhibits great thickening of the intima, and if the section is examined more highly magnified it is seen that the tissue of the intima contains many of the same hollowed cells visible in the intima of the vessel shown by Fig. 93. The muscularis, which requires higher amplification to distinguish very clearly, is in close contact with the surrounding fibrous tissue, and there is no trace of any separation of the adventitia of the vessel from the tissue of the trabecula in which it lies. The appearance exhibited by this vessel (Fig. 94) and by Fig. 93 is exceedingly common in the spleen. This condition of the blood-vessels is frequently found in the bodies of persons dead of almost every kind of disease, and it is especially apt to be found in those who have died of Bright's disease —which both of these patients had, although in the case of the man from whom Fig. 94 was obtained the kidney disease was apparently an incident in the course and progress of the myelitis from which he died. However, it would be difficult to prove whether the myelitis or the contraction of the kidney started first, for the symptoms of disease of the spine manifested themselves, but there never were any symptoms of the disease of the kidney.

In conclusion, it may be said that it might have been expected that the study of the blood-vessels of the spleen would prove inconclusive, since the function of the organ remains unknown and there is still much to be learned of its anatomy. It is something, however, to know that its arteries are prone to be affected by endarteritis of the same character as that which attacks those of other organs and tissues, and that this disease of the intima of the arteries of the spleen occurs at almost all periods of life and in persons dead of almost every disease.

CHAPTER XII

The Blood-Vessels of the Kidney

The blood-vessels of the kidney have probably been more extensively studied than those of any other organ. I have myself examined a greater number of them than of any others except those of the heart, of which I have made a special study. Although this is the case, I have less to say about the kidney than has been said of the other organs, both because the anatomy of the blood-vessels of the kidney is better known and because a good many drawings of blood-vessels of the kidneys have been included in other chapters of this work, as they illustrated points connected with the subjects of those chapters. The general anatomy of the kidney is better understood than that of most organs, and there is no good reason to suppose that very much remains to be discovered in regard to the circulation of the blood in the kidney. Its flow has been thoroughly traced from its entrance by the renal arteries to its departure by the veins. The ramifications of the capillaries among the tubules and the entrance of the afferent and the exit of the efferent vessels of the Malpighian tufts and the convolutions of the intervening capillary loops have been seen in every stage of their course. Although the circulation seems in some respects to be complicated, it is arranged upon a very simple plan. Two statements may be made with regard to the kidney: first, no text-book contains an accurate description or illustrations of perfectly normal renal blood-vessels, any more than of the blood-vessels of the other organs, and therefore any one who studies disease of the kidney is constantly confronted with the difficulty of deciding whether a particular blood-vessel is normal or diseased; and, second, the blood-vessels of no other organ are so prone to be affected by endarteritis as those of the kidney, unless the disease is even more common in the heart. The very commonest morbid appearance of kidney which has undergone fibroid or almost any other form of chronic degeneration is that the blood-vessels, and especially the arterioles, are thickened inwards. Frequently this thickening of the intima is so great that the affected vessels are nearly closed. The appearance of

a blood-vessel diseased in this manner is entirely different from that of a normal vessel. The normal vessels in cross-sections are seen to be thin-walled, with relatively large lumina, while those which are diseased are thick-walled and the openings are small—often so small as to be insignificant. Whether disease of the blood-vessels of the kidney attacks them early, and stands in a causative relation to the other lesions which generally accompany it, or is only an effect, has not yet been discovered. It is perfectly well known by anatomists, but is not so generally known as it should be, that the kidney of the adult man is supplied with blood not by the renal arteries alone, but also by small arterioles which pass through the capsule of the kidney and enter the organ from the outer curved surface.

Fig. 95 is a cross-section of an artery extending from the perirenal fat through the capsule into the kidney of a man seventy years old who died of chronic myelitis. It is a fully developed artery like any other, it has three coats,—adventitia, muscularis, and intima,—and the plicated membrane is easy to see. This artery, however, as were many of the other arteries of the same kidney, is diseased. The adventitia is normal; the muscularis is unevenly thick, but this is not of great degree; the intima is very much thicker than is normal and it is unevenly thick. A curious and unusual feature is the situation of the plicated membrane, which, instead of forming the boundary between the muscularis and intima, as it ordinarily does, is in places directly in the middle of the intima. This is a condition that I have not seen before, although I have examined a great many arteries. Ordinarily the plicated membrane is directly in contact with the muscularis around its entire circuit, and this situation of the plicated membrane renders it easy to distinguish to which of the coats disease belongs. The nearest approach that I have seen to a condition like this is exhibited by Fig. 10, "Origin of Disease." The plicated membrane of the artery represented by that drawing is split in two, and one of the split ends extends into the intima instead of lying between the muscularis and the intima. Both the thickening of the intima and the unusual situation of the plicated membrane in the middle of the intima shown by Fig. 95 must be the results of disease. At present the record of such facts as these seems almost useless, for it is impossible now to know what the disease means, what causes it, or if it has any consequences which are of importance. The record appears especially

useless, perhaps, because the artery is one of those which pass through the capsule of the kidney to enter the organ from its outer curved surface. Little attention has been paid to this system of blood-vessels by anatomists, and as yet none at all has been paid to their diseases. Recently an operation has been advocated for the removal of the capsules of fibroid kidneys, and it has been claimed that it aids to establish a collateral circulation and thus to cure cases of contracted kidney. In my book on the "Origin of Disease" one of these arteries distributed to the surface of the kidney is depicted by Fig. 107, and at page 132 I described its peculiarities, and mentioned the fact that it is almost certain that these arteries are not developed in the embryo, but are a post-embryonic growth. The general question, to what extent development continues after birth in the higher animals, and the particular one, at what time the vascular supply to the surface of the kidney is formed, are interesting and very likely of importance, but at present they are both quite unanswerable.

Fig. 96 shows a diseased blood-vessel and Malpighian bodies of the contracted kidney of a woman forty-two years old who died of cerebral apoplexy. Most of the results of fibrosis and contraction of the kidney are well known and many of the effects are depicted in text-books, for this subject has been most extensively studied. The drawing is therefore intended only to emphasize what is already known. There are three Malpighian bodies which are so changed by disease that from their appearance alone it would be quite impossible to recognize them. They are masses of fibroid tissue with nuclei, and in one of them two capillaries can still be distinguished. The blood-vessel is probably a diseased arteriole. It is a mass of fibroid material containing nuclei, and there is a small eccentrically placed opening which is the lumen. Around the Malpighian bodies and diseased blood-vessel which lie in a degenerated fibrous portion of the kidney, are scattered kidney tubules which were cut in various directions. Fig. 96 affords a striking illustration of what happens to the smaller blood-vessels of contracted kidneys. Not only has the small arteriole been converted by the disease almost entirely into fibrous tissue, but the Malpighian tufts, which when normal are composed of little else but capillaries, are turned into dense balls of fibrous tissue, hardly a trace of the capillaries remaining.

FIG. 95.—ARTERY EXTENDING FROM PERINEAL FAT INTO KIDNEY. (× 50.)

From a man seventy years old who died of chronic myelitis. It is a fully developed artery, having three coats and a distinct plicated membrane. Like most blood-vessels of old people it is not like the standards of the normal, for the intima is thicker than is considered to be natural in so small an artery, and the plicated membrane is in places in the middle of the intima instead of forming the boundary between the intima and muscularis, as is usual. This latter is an unusual feature and is difficult to explain.

FIG. 95.

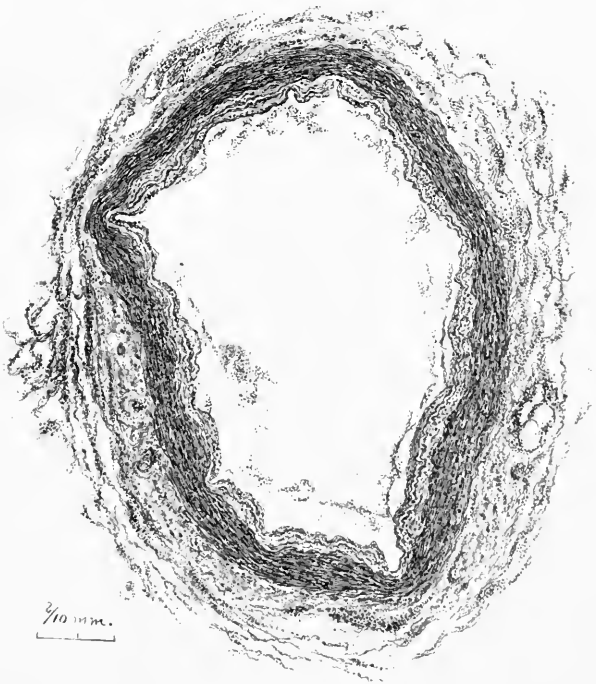
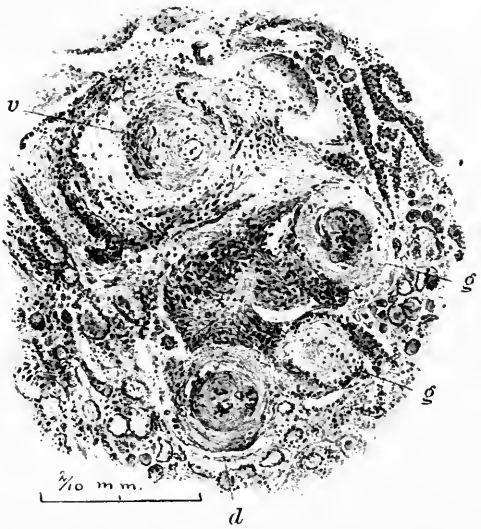


FIG. 96.—DISEASED BLOOD-VESSELS OF FIBROID KIDNEY. (× 105.)

From a woman forty-two years old who died of cerebral apoplexy. The section is from the cortical portion of a very contracted kidney. *g*, *g*, two Malpighian bodies which have undergone fibroid contraction to such an extent that no trace of the capillaries can be distinguished; *d*, a fibroid Malpighian body in which the openings of two capillaries can be seen; *v*, a blood-vessel. It is probably an arteriole in which the intima was thickened to such an extent as to produce the effect that is seen. The lumen is very small; it is not centrally placed, and the wall of the vessel has lost all of the ordinary cellular structure and differentiation of three coats. Such changes are very common in arterioles of this size.

Fig. 96.



My discussion of the subject of the blood-vessels of the kidneys is very incomplete and perhaps unsatisfactory, but so much has been written of it by others, and I have already recorded so much regarding it in the chapters on the kidney and on the blood-vessels in my book on the "Origin of Disease" and in various of the other chapters of this work, that it has not seemed to me to be desirable to include more here than the brief record I have made, and to reiterate, in conclusion, that the studies of the blood-vessels of the kidney and of the heart have been more thorough and the results more satisfactory than can be said to be the case concerning those of any of the other organs or tissues.

CHAPTER XIII

The Blood-Vessels of the Brain and Spinal Cord

The blood-vessels of the brain and spinal cord and their diseases have already been discussed and drawings of them have been included in Chapters I and IV. It is undesirable to repeat to any extent what has already been said, and yet a certain amount of repetition may be unavoidable. Most of the blood-vessels of the brain and spinal cord, and all of the largest ones, are situated in the membranes outside the actual nerve-tissue, for only small vessels penetrate the nerve substance itself. The greater number of the vessels and all of the large ones are suspended in the loose tissue of the meninges, and are therefore without any external support like that which is afforded by surrounding tissue to those within the substance of the liver, kidney, and heart, and even of the lung, although the latter organ is of a light and spongy consistency. In this respect the large vessels of the nervous system resemble the main arterial and venous trunks, which are generally situated in the cavities and spaces of the body in such a manner that they also are suspended by the perivascular connective tissue, and are without support from any surrounding solid tissue. It seems to me that the blood-vessels of the brain and of the spinal cord are less frequently affected by endarteritis than the vessels of many other parts, especially those of the thoracic and abdominal viscera and the large arterial trunks such as the radial and femoral and even the aorta. In my experience it has been comparatively rare to find blood-vessels of the nervous system with thick walls and small calibres like those, for instance, which are so common in the kidney and in the heart. Cerebral hemorrhage is one of the most frequent causes of death in persons past fifty years of age. It may be that part of the reason for this is because the arteries of the brain are less liable to thickening of their walls than those of other tissues. In my book on the "Origin of Disease," at page 172, I expressed the opinion that cerebral hemorrhage is due to ulceration of the lining of the arteries, which produces gradual thinning of the walls, until finally rupture takes place as a result of the ulceration, and that strain and

violence generally do not have any influence in precipitating the rupture and hemorrhage. If this be true, the process is exactly similar to what occurs in perforation of the intestine in typhoid fever. It may be that if the thickening of the blood-vessels which occurs with advancing years is a partially conservative process, and if the vessels of the nervous system were more subject to it, death from cerebral hemorrhage would be less frequent.

Fig. 97 is an illustration of an artery and a venous capillary from the brain of a girl eighteen years old who died of typhoid fever. They are from the surface of the cerebrum, and it is fair to assume that they are natural. The artery occupies the centre in the drawing, and it is filled with blood-corpuscles; its wall is normal. The venous capillary is above the artery, and the curious feature shown by the drawing is that the accompanying return vessel of an artery of such considerable size may sometimes be a capillary in structure instead of being a vein. The wall of the vessel is formed of a very thin layer of fibrous tissue which contains nuclei. There is nothing resembling a division into three coats, nor is there a trace of muscular tissue in the wall of the vessel. This fact, that the accompanying return vessels found with arteries sometimes are capillaries, is well known to anatomists, but it is not so generally known as it should be. The subject is discussed in Chapter I, and Fig. 18 represents a pair of the vessels from the spinal cord.

Figs. 98 and 99 depict an artery and a venous capillary from the spinal cord of a woman twenty-six years old who died of typhoid fever. The artery is natural, and the venous capillary exhibits much the same character as Fig. 97. The wall of this capillary is formed of fibrous tissue and there is nothing like the division into three coats which is characteristic of normal veins. As these two vessels are a good deal larger than those represented by Fig. 97, their walls are naturally much thicker. This anatomical arrangement, where the capillaries which perform the function of returning the blood to the heart are of so much greater size than any of the ordinary capillaries which are occupied in the work of supplying blood to the tissues, is a curious one, and it will very probably some day be discovered to have an important influence in the production of disease or in determining its course. In Chapter VIII the large capillaries that exist in the heart are described and they are represented by drawings.

Fig. 100 shows a blood-vessel of the spinal cord of a woman of twenty-six years who died of typhoid fever. It is not one of the vessels of the meninges, but lay within the spinal cord. This is shown by the drawing, for the nerves are cut across and lie adjacent to the vessel upon either side of it. The appearance of the vessel is one which is not rare in the brain and spinal cord, but it is one I am quite unable to explain, nor can I even say whether it is natural or is due to disease. There are many blood-corpuscles lying in the lumen of the vessel. The walls are not like those of any of the normal blood-vessels. They are composed of an outer and an inner layer of dense fibrous tissue, between which is tissue that is also fibrous but is much less dense. The lines of the fibres in this vessel all run longitudinally. The blood-vessel cannot be classified as an artery nor as a vein, and if it be a capillary it is not like any of the normal ones as they are ordinarily described. It is possible that the condition depicted may be the result of typhoid fever, of which disease the patient died. In typhoid fever the tissues are often very much softened, and the walls of the vessel might have become swollen owing to exudation of the nature of œdema.

Fig. 101 shows an artery of the circle of Willis at the base of the brain of a negro man seventy-four years old who died of hemiplegia. The artery is very much degenerated. The adventitia and muscularis are readily distinguished, and it is easy to see that both are thinner than is usual in arteries of their size. The reason for this is not evident. All the tissue that lies inside of the muscularis is intima, and it is very much thickened and degenerated. Greater amplification than was used shows more of the details of structure and of the degeneration, but a great deal is shown by the drawing. There are many cavities in the tissue, and a glance reveals that it is almost disintegrated, for it is quite unlike the well-organized tissue which forms the intima in most thickened arteries. It was said in the earlier part of this chapter that endarteritis is less common in the brain and spinal cord than in some of the other tissues. The appearance of this vessel shows that the condition does occur even if it is not so common. However, much as the arterial wall is thickened, it is but little so in comparison with what occurs in the arteries of other parts. The state of disease exhibited by this artery is interesting as showing what may be found in the large arteries of the base of the brain of an old man dead of hemiplegia.

FIG. 97.—NORMAL ARTERY AND VENOUS CAPILLARY OF THE BRAIN. (× 105.)

From the cerebrum of a girl eighteen years old who died of typhoid fever. The artery is below and its lumen is filled with blood-corpuscles. The venous capillary, which is directly above the artery, has the character of ordinary capillaries. Its wall is a fine thread of endothelium containing nuclei. The striking feature is that the accompanying venous vessel of such a good-sized artery should be a capillary.

FIG. 98.—ARTERY OF THE SPINAL CORD. (× 50.)

From a woman twenty-six years old who died of typhoid fever. It appears to be normal.

FIG. 99.—VEIN OF THE SPINAL CORD. (× 50.)

From the same case as Fig. 98. It is probably normal. The noticeable feature is that the wall of the vein is simply a ring of fibrous tissue, there being no division into adventitia, muscularis, and intima, as the ordinary histological descriptions portray veins of its size.

FIG. 97.

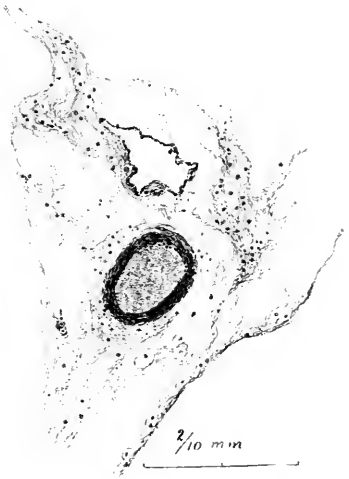


FIG. 98.

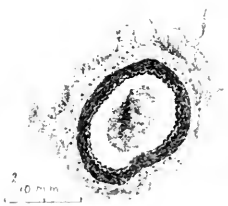


FIG. 99.

FIG. 100.—BLOOD-VESSEL OF THE SPINAL CORD. (× 240.)

From a woman of twenty-six years who died of typhoid fever. There are many blood-corpuscles lying within the lumen of the vessel, and outside of it are seen the nerve-fibres of the cord. The vessel wall is composed of an inner and an outer line of fibrous material with a layer of lighter tissue between them. There is no muscularis or intima.

FIG. 101.—DISEASED ARTERY FROM THE CIRCLE OF WILLIS. (× 20.)

From a negro man seventy-four years old who died of hemiplegia. *a*, adventitia; *m*, muscularis; *c*, a clot lying within the lumen of the artery. The adventitia and muscularis compose a small part of the total thickness of the vessel wall. All of the tissue lying within the muscularis is the intima, which is disintegrated and full of cavities produced by disease. Examined with higher power it can be seen that much of the tissue of the intima is structureless owing to the extensive disintegration.

FIG. 100.

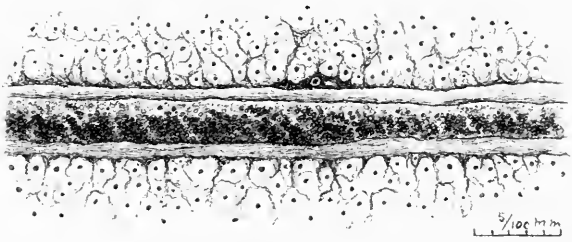


FIG. 101.

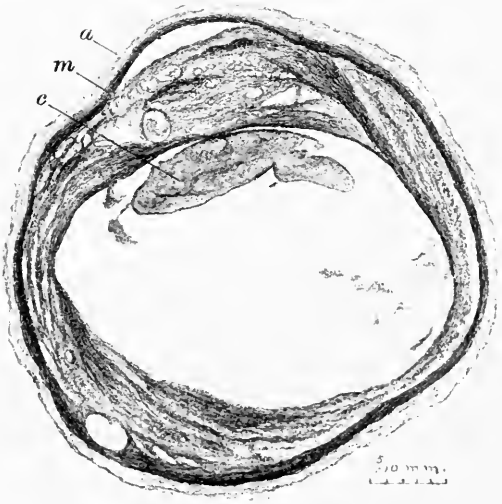


Fig. 102 gives a representation of the basilar artery and a small arteriole of a man thirty years old who died of hemiplegia, the cause of which was thought to be syphilis, but this diagnosis could not with certainty be established. A number of curious things are shown by the drawing. The basilar artery is entirely filled by a clot which was easily seen with the unaided eye before the vessel was cut and prepared for microscopical examination. At page 12 it is stated that during life the plicated membrane is straight and that its folds are the result of post-mortem shrinkage, and there are illustrations to show how differently it appears in different sections of the same artery if some pieces are allowed to shrink unobstructed in the course of preparation for microscopical examination and others are prepared with rigid glass rods in their calibres to prevent shrinkage. This diseased basilar artery, which is filled with an organized clot, demonstrates the correctness of the opinion that the folds of the plicated membrane are due to post-mortem shrinkage. The clot is so large and so firm that it has done exactly what the glass rods did in the vessels in which they were placed in the experiments to which allusion has been made,—post-mortem shrinkage was to a great extent prevented, because the calibre of the artery was filled by the clot. To the left in the drawing the plicated membrane is easily seen, although to the right it cannot be distinguished at all, as it has been destroyed by the disease. No part of the plicated membrane that remains is folded as much as it usually is in vessels prepared as this one was, but the lower portion of it shows the corrugated or wavy appearance quite distinctly, while above it appears as a perfectly straight glassy membrane. The straight portion is exactly like what is shown by Fig. 11. It is singular that disease should have filled the lumen of this artery with clot so as to reproduce almost exactly the conditions obtained by my experiments of preparing pieces of arteries with glass rods in them to prevent shrinkage. An interesting process shown by this artery is organization of clot and its relation to the tissue of the arterial wall. To the left the adventitia, the muscularis, and the plicated membrane are perfectly distinct and are easy seen, but at other parts of the large irregular circle or oval formed by the vessel they cannot be distinguished. If the muscularis upon the left is followed upward with the eye, it is seen to form an angle which must have been caused by shrinkage, and a little beyond this point as it passes toward the right

it widens somewhat and then disappears into a mass of diseased tissue. In this region it is impossible to recognize any difference between the tissue which forms the arterial wall and the clot which fills the lumen of the vessel. This is distinctly shown by the drawing, but if the section be examined under greater amplification still more details of the structure can be recognized. The manner in which the vessel wall and the clot merge together is surprising. At the central portion the clot is yellowish and it is formed of partially disorganized blood, at the periphery the tissue of the arterial wall is distinct, but between these two extremes a great part of the material is of such a nature that it is impossible to say whether it is arterial wall or clot, and it is quite impossible to draw a line showing where natural tissue ends and clot begins. The condition of disease exhibited and that of organization of clot are sufficiently common, but the drawing shows them unusually well.

Fig. 103 shows the small arteriole *b* in Fig. 102. The disease was, as has already been said, probably syphilis. It is perfectly evident that the vessel is not normal, but the only abnormality that can be distinguished is infiltration. The muscularis is easily recognized, and at its upper portion there is a thick layer of infiltrated tissue inside of it; at the lower portion there is a large area of infiltration, but this lies outside of the muscularis, and it looks therefore as if the infiltration had had its origin in the adventitia or entirely outside of the blood-vessel, in the perivascular tissue. Syphilitic and tubercular disease of arteries have been described, and it has been thought by some that they could be recognized by their appearance without regard to the clinical history of the patient or to other lesions. There cannot be any doubt that inflammation also is capable of producing arterial disease. It is my belief that syphilis, tuberculosis, and inflammation produce effects upon the arteries which in their microscopical appearances are identical. These diseases are therefore indistinguishable unless the clinical history of the patient or something in the gross appearance of the lesions tells which of the three is present. The lesion which is common to the three diseases is cell infiltration. This effect is characteristically shown by Fig. 103, which depicts an arteriole of a man thirty years old who died of hemiplegia. The hemiplegia was, of course, not due to the clot in the basilar artery, and there is no positive proof that the disease was syphilitic; but the

FIG. 102.—DISEASED BASILAR ARTERY OCCLUDED BY CLOT. (× 20.)

From a man thirty years old who died of hemiplegia (probably syphilitic). *b*, a blood-vessel represented more highly magnified by Fig. 103. *m*, muscularis, which towards the other side of the artery becomes indistinguishable, for it merges into the diseased tissue and the clot. *p*, plicated membrane. Parts of it are folded, as usual, and other parts are straight, owing to the fact that the lumen of the artery is filled with clot which distends it and prevented the usual post-mortem shrinkage. *e* is a region where the wall of the artery and the clot come together and have commingled so that it is impossible to distinguish where the clot ends and the tissue begins. It is a good exemplification of the organization of clot.

FIG. 103.—INFLAMMATION OF A BLOOD-VESSEL. (× 50.)

Enlarged view of the blood-vessel *b* in Fig. 102. The case was probably one of syphilis. The appearance is identical with the disease commonly described as tubercular arteritis. *m* is the muscular coat and it can be distinguished all the way around the vessel. At the top it is most distinct, and below it is obscured by the cellular infiltration which has resulted from the process of inflammation.

FIG. 102.

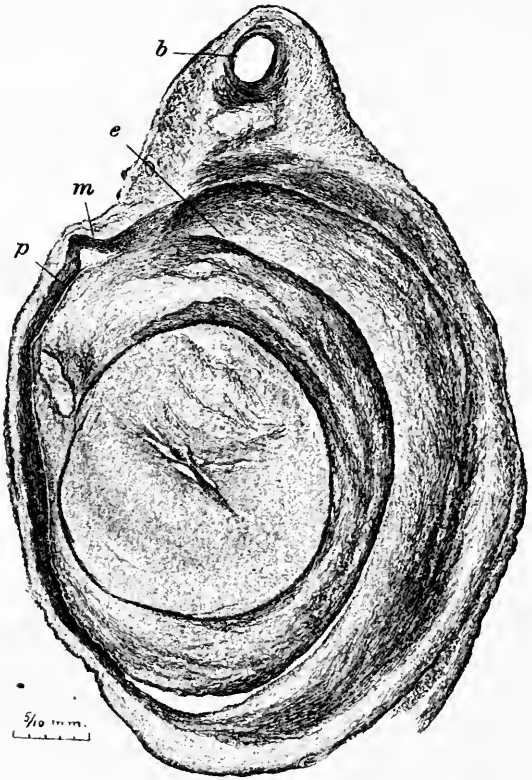
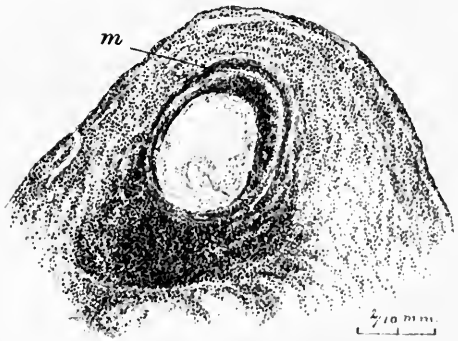


FIG. 103.



clinical evidence seemed to point that way and, besides, syphilis is the most frequent cause of hemiplegia in young persons. In my book on the "Origin of Disease," Fig. 33 represents an arteriole from a tuberculous area of the lung, and at page 58 of that book it is asserted that the disease which is shown by the drawing is an overwhelming cell infiltration which looks as if it had had its origin in an invasion of the blood-vessel wall from the outside, and it is further said: "tubercular arteritis, therefore, has no real existence, and the condition is nothing but the involvement of the vessels by the cellular infiltration which is characteristic of the tubercular process everywhere." The appearance of the arteriole lying in the very midst of a tuberculous portion of lung is identical with that of Fig. 103, although the diseases were clinically so different and the one arteriole was from the lung and the other from the brain. In both instances the appearances tend to make one think the disease had its origin in the tissue around the vessels and included them in the course of its progress rather than that it was really of vascular origin. It is a matter of common knowledge to those who have studied pathological histology, that in any tissue which is subjected to the process of inflammation, as cellular infiltration increases and takes in more territory in the course of its progress, the blood-vessels of the invaded tissue are infiltrated by the cells just as all of the rest of the tissue is, and that this infiltration attacks first the adventitia and then proceeds through the muscularis, the intima, and, finally, if the inflammation is sufficiently active, the lumen of the vessel is filled by the cells, and in the end all sign of the blood-vessel disappears, its place being taken by a mass of cells. The two arterioles that have been described, the one from a tuberculous portion of lung and the other from the brain of a man who died of hemiplegia which was probably syphilitic, show that in the two dissimilar diseases similar lesions resulted. It cannot be doubted that inflammation can produce the same disease of blood-vessels, and therefore it is no more than just to say that the three conditions of disease—tuberculosis, syphilis, and inflammation—may produce identical histological changes of the blood-vessels.

In conclusion, it seems best to repeat that a great deal that has been included in this book is of an unsatisfactory nature and does not lead to any definite result. This has been unavoidable, for the reason that many of the illustrations—and it is upon the illustrations to a

large extent that the book is founded—are of conditions that I am quite unable to explain. Such illustrations were included, however, in the hope that the day may come when their peculiarities will be explained and that they may then be of value. The subject of the microscopical anatomy of the blood-vessels has not yet been sufficiently studied to make the record of it satisfactory and the pathology of the blood-vessels is but little understood. If my record adds anything to the knowledge of the anatomy of the blood-vessels or of their diseases, it will have fulfilled the purpose for which I made it.

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