ABBOTT SMITH PAYN, M.D.....New York, N. Y.

W. F. R. PHILLIPS, M.D..... Washington, D. C.
United States Weather Bureau.

NORVAL H. PIERCE, M.D.....Chicago, Ill.
Professor of Otology, Chicago Polyclinic; Laryngologist and Aurist to the Michael Reese Hospital, the Chicago Orphan Asylum, and the Passavant Memorial Hospital; Aural Surgeon, Illinois Charitable Eye and Ear Infirmary.

N. J. PONCE DE LEÓN, M.D.....Havana, Cuba.
Lately Assistant Visiting Physician, Department of Diseases of Children, Dispensary of Cornell University Medical School in New York City.

WILLIAM H. PORTER, M.D.....New York, N. Y.
Professor of Pathology and Medicine, New York Post-Graduate Medical School; Curator of the Presbyterian Hospital; Pathologist to the Northern Dispensary.

CHARLES E. QUIMBY, M.D.....New York, N. Y.
Clinical Professor of Medicine, the University and Bellevue Hospital Medical College; Visiting Physician, City Hospital.

OTTO G. RAMSAY, M.D.....New Haven, Conn.
Professor of Obstetrics and Gynæcology, Medical Department, Yale University; Obstetrician to the New Haven Hospital.

HUNTINGTON RICHARDS, M.D....Concord, N. H.

HENRY H. RUSBY, M.D..... Newark, N. J.
Professor of Botany, Physiology, and Materia Medica, New York College of Pharmacy; Professor of Materia Medica, University and Bellevue Hospital Medical College.

EDWARD W. SCHAUFFLER, M.D. Kansas City, Mo.
Professor of Principles and Practice of Medicine, Kansas City Medical College.

R. J. E. SCOTT, M.D.....New York, N. Y.
Attending Physician, Out-Patient Department, Bellevue Hospital; Assistant Gynæcologist, Demilt Dispensary, New York.

CARL SEILER, M.D..... ....Scranton, Pa.

FRANCIS J. SHEPHERD, M.D. .Montreal, Canada.
Professor of Anatomy and Lecturer on Operative Surgery, Medical Department, McGill University; Senior Surgeon, the Montreal General Hospital.

ARTHUR M. SHRADY, M.D.....New York, N. Y.
Instructor in Physical Diagnosis, Medical Department of Columbia University; Attending Physician, Seton Hospital.

BEAUMONT SMALL, M.D.....Ottawa, Canada.
Attending Physician, St. Luke's General Hospital, Ottawa; Consulting Physician, the Children's Hospital; Late Examiner in Materia Medica, College of Physicians and Surgeons, Ontario.

ANDREW HEERMANCE SMITH, M.D. .New York, N. Y.
Attending Physician, Presbyterian and Post-Graduate Hospitals; Consulting Physician, St. Luke's, St. Mark's, Ruptured and Crippled, and Woman's Hospitals.

HENRY RUST STEDMAN, M.D.....Boston, Mass.
Superintendent, Private Hospital for Mental and Nervous Diseases, Roslindale, Mass.

THOMAS L. STEDMAN, M.D.....New York, N. Y.

H. S. STEENSLAND, M.D.....Syracuse, N. Y.
Lecturer on Pathology, College of Medicine, Syracuse University; Pathologist to St. Joseph's Hospital, the Hospital of the Good Shepherd, and the Hospital for Women and Children.

ALFRED STENGEL, M.D.....Philadelphia, Pa.
Instructor in Clinical Medicine, Medical Department, University of Pennsylvania; Physician to the Philadelphia and the Children's Hospitals.

GEORGE D. STEWART, M.D.....New York, N. Y.
Professor of Anatomy and Clinical Surgery, the University and Bellevue Hospital Medical College; Visiting Surgeon, Bellevue Hospital; Adjunct Visiting Surgeon, St. Vincent's Hospital.

EMANUEL J. STOUT, M.D.....Philadelphia, Pa.
Instructor in Dermatology, Jefferson Medical College; Associate Physician, Northern Dispensary, Department of Skin Diseases.

GEORGE C. STOUT, M.D.....Philadelphia, Pa.
Instructor in Diseases of the Ear, Philadelphia Polyclinic; Assistant Demonstrator of Histology, Medical Department, University of Pennsylvania.

SAMUEL THEOBALD, M.D.....Baltimore, Md.
Clinical Professor of Ophthalmology and Otology, Johns Hopkins Medical School; Surgeon to the Baltimore Eye, Ear, and Throat Charity Hospital; Ophthalmic and Aural Surgeon, the Johns Hopkins Hospital.

BENJAMIN T. TILTON, M.D.....New York, N. Y.
Instructor in Surgery, Cornell University Medical College in New York City; Assistant Visiting Surgeon, Bellevue Hospital; Visiting Surgeon, Lincoln Hospital, New York.

HARRY ASHTON TOMLINSON, M.D....St. Peter, Minn.
Physician-in-Chief and Superintendent, St. Peter State Hospital.

GEORGE THOMAS TUTTLE, M.D..Waverley, Mass.
First Assistant Physician, McLean Hospital, Waverley, Mass.

FREDERICK H. VERHOEFF, M.D....Boston, Mass.
Pathologist, Massachusetts Charitable Eye and Ear Infirmary; Assistant in Pathology, Harvard University Medical School; Assistant Ophthalmic Surgeon, Carney Hospital, Boston.

HENRY BALDWIN WARD, Ph.D....Lincoln, Neb.
Professor of Zoölogy, University of Nebraska; Zoölogist of the State Board of Agriculture.

JOSEPH W. WARREN, M.D.....Bryn Mawr, Pa.
Associate Professor of Physiology, Bryn Mawr College.

ALDRED SCOTT WARTHIN, M.D.....Ann Arbor, Mich.
Junior Professor of Pathology, Medical Department, University of Michigan.

H. GIDEON WELLS, M.D. .....Chicago, Ill.
Associate in Pathology, University of Chicago.

GROVER W. WENDE, M.D.....Buffalo, N. Y.
Clinical Professor of Dermatology, University of Buffalo Medical School; Physician for Diseases of the Skin at the Erie County, Buffalo Sisters of Charity, and German Hospitals.

WILLIAM A. WHITE, M.D.....Binghamton, N. Y.
First Assistant Physician, Binghamton State Hospital.

ROYAL WHITMAN, M.D..... New York, N. Y.
Chief of Clinic and Instructor in Orthopedic Surgery, Medical Department, Columbia University.

ALFRED C. WOOD, M.D.....Philadelphia, Pa.
Demonstrator of Surgery and Instructor in Clinical Surgery, Medical Department, University of Pennsylvania; Assistant Surgeon, Hospital of the University of Pennsylvania; Surgeon to the Philadelphia, St. Timothy's and St. Agnes' Hospitals, Philadelphia.

FRANCIS CARTER WOOD, M.D..New York, N. Y.
Instructor in Clinical Pathology, Medical Department, Columbia University; Pathologist to St. Luke's Hospital, New York.

ALFRED A. WOODHULL, M.D., LL.D. .Princeton, N. J.
Colonel, United States Army, Retired; formerly an Assistant Surgeon-General.

* Deceased since the issue of the first edition.

A REFERENCE HANDBOOK

OF

THE MEDICAL SCIENCES.

INFLAMMATION.—Under the term inflammation may be understood the changes which take place in a tissue on the receipt of an injury, including not only those immediately produced by the injurious agent acting directly on the tissues but also the more remote changes. Such a definition strictly carried out would include the special pathology of organs, because in every organ the process may be modified by variations in structure and function. It would include the study of all injurious agents, and among them the bacteria and the changes which these severally may produce. Even malformations would not be excluded because most of these are due to injurious conditions or agents, acting on the embryo and influencing or preventing development. Tumors might possibly not come within the meaning of the word, though even here there is a possibility that the growths may be referred in part to the action of injurious agents acting on the tissues of the embryo or the adult. In fact all pathology is but a study of injurious agents or conditions and their effects. There are so many conditions produced by injury and some of them are so complicated that it has been proposed to exclude any word descriptive of the whole and to consider the different conditions separately. In this article I shall attempt to give a general description of the most common conditions which are produced by injury. These conditions are so modified by the character of the injurious agent, the structure of the tissue it acts upon, and the greater or less resistance of the individual, that a general description certainly cannot fit all cases, and it may not be true in its entirety in even a single instance. With the extension of our knowledge of pathological processes, or rather with the substitution of knowledge for conjecture, the difficulty of general description increases. Even in the experimental study of injuries, when all the conditions can be controlled to a great extent, it is difficult to produce exactly the same lesion, in the same tissues, under apparently the same conditions.

When a tissue is placed under the action of abnormal conditions it undergoes injury and probably in all cases structural alterations are produced in it. In some cases these structural alterations are easily recognized and come under the head of the various degenerations. In other cases we must assume the alteration from the change in function which follows. There is a very different degree of vulnerability in the different tissues of the body, and some may be destroyed by causes which produce no effect upon others.

It is very rare that single elements in a tissue are alone affected by the injurious agent, though in a complex tissue the different elements may have different degrees of vulnerability, and the injurious effects are then more marked in some elements than in others. We usually find changes in all the constituents of a tissue, some of which may be due to the action of the primary cause, while others are secondary and due to the changes which the acting cause has produced. Any injury to a tissue must influence its nutrition, and so intimate is the association between the circulation and the nutrition of a part that any influence affecting the nutrition will produce changes in the character of the circulation. The vessels in a tissue may be immediately influenced by the primary action of the injurious agent, but the influence of this agent extends far beyond this. In non-vascular tissues which are nourished solely by lymphatic channels, the vessels from which the nourishing lymph passages are supplied show changes of the same character as the vessels which are supposed to be immediately affected by the injury. In some cases we are not able to see in what way this influence extends to the vessels. The only way in which it is possible to study the effect of injurious agents on the cells alone is in the unicellular organisms. Few of the changes which we see in these organisms have any analogy with those seen in higher animals. The power of regeneration of the protoplasm is infinitely greater, and the single cell can perform all the functions which in higher animals are relegated to a great many tissues and cells.

In most tissues of the body and in most situations the injury is followed by certain changes which are partly subjective and partly objective, and the more conspicuous of these have been singled out and regarded as the cardinal symptoms or signs of inflammation. These are heat, redness, swelling, and pain. The presence of these signs and their degree, as a whole or considered singly, depend upon a great many factors. Increased heat in the area affected, which is such an important sequence of an injury on the external surface of the body, will be entirely absent in an internal organ. Redness will be absent in a non-vascular tissue, and even in a vascular organ the part most affected by the injury may often be recognized by its pallor. The degree of swelling will depend upon the character of the tissue, and its greater or less capacity for distention; it may be absent, or be present to a greater degree in an adjoining tissue which was not immediately affected by the injury. Pain is a wholly subjective phenomenon and its presence and intensity depend not only upon the character of the tissue which is affected but also upon the individual.

These phenomena can best be studied by producing varying degrees of injury in some vascular tissue which is capable of continuous observation. The ear of an albino rabbit is admirably adapted for this purpose. The whole series of changes may be produced by immersing the ear in water of 53° C. for three minutes. By varying the duration of immersion or the temperature of the water any degree of injury up to complete destruction of the tissue may be produced. Variations of a degree in the temperature of the water will have a marked difference in the result. At the beginning of the immersion close observation may show a slight pallor of the ear which soon gives place to redness. The redness is perceptible on withdrawing the ear from the water, and it gradually increases; even in the beginning it exceeds the redness produced by the physiological vascular dilatation. Arteries and veins are dilated as compared with the normal ear and the homogeneous redness shows the dilatation of the capillaries. The red has a bright, almost arterial

color in the beginning, but this in a few hours gives place to a dusky red color. If the immersion has extended to only the upper half of the ear, the general intense redness will extend slightly beyond the area of immersion; but the dilatation of the large vessels, both arteries and veins, will be seen in the lower half of the ear. On taking hold of the two ears increased pulsation can be felt in the injured ear, and on noting the temperature of the injured ear it will be found from 1° to 3° C. warmer than the normal. In addition to the general diffuse redness there may appear small, intensely red foci which, unlike the diffuse redness, cannot be made to disappear on pressure. Another very striking phenomenon is that the periodic flushing of the ear due to the alternate contraction and dilatation of the arteries is absent in the injured ear; the redness is continuous. It is perfectly evident from this that immediately following the injury there is dilatation of the arteries, and more blood is brought to the ear and more flows through it and is discharged by the dilated veins. The increased rapidity of flow is shown in the bright color approaching that of arterial blood, and in the increased temperature, the blood in the rapid circulation losing neither its oxygen nor its heat. The small red foci mark minute blood extravasations in the tissue. If the experimenter expose his hand to water of the same temperature the same phenomenon will be observed. By allowing the hand to remain in the water for periods varying from a few moments to one sufficiently long to induce distinct pain, different degrees of hyperæmia will be produced. It is temporary if the immersion has been short, or may continue for some hours if the immersion has been for a longer time. There is also a sensation of increased warmth and of increased fulness and tension in the hand. Continued observation of the ear shows another change which develops more slowly than the redness: the ear becomes swollen. The swelling begins to appear a few hours after the immersion and increases in degree up to twelve hours or longer, dependent upon the degree of the injury; it finally becomes so great that the animal is no longer able to keep the ear erect. There is a general diffuse swelling and on the inner surface of the ear are seen small blebs filled with a fluid which has come from the tissue and pushed up the horny layer of the epidermis before it. These blebs often rupture, and crusts are found on the surface due to the drying of their contents. With this swelling of the tissue there is evidently pain, for the animal shows uneasiness when the ear is handled and avoids contact with surrounding objects.

The actual condition of the tissue may be seen on microscopical examination. Small pieces of the tissue can be cut out and instantly killed by placing them in corrosive sublimate or in Zenker's fluid. The normal ear shows in the middle a thin lamella of hyaline cartilage with a thin perichondrium on each side of this. In the lower part of the ear there is a thin layer of striated muscle. Then comes on each side a layer of fibrous tissue which is thicker on the outside of the ear, and in this the hairs and their glandular appendages are embedded. On the inside of the ear the hairs are small and few in number and there are a few small glands not connected with the hairs. Twelve hours after the immersion the section may be twice as thick as the normal, or more. The thickness is most marked on the outside of the ear and is due to swelling of the connective tissue. The fibres in this are separated and often some granular coagulum is seen between them. A much greater number of cells is found in the tissue. The cells are most numerous on the inside of the ear, and on both sides are chiefly collected beneath the epidermis. Numbers of them will also be found within the small blebs on the inner surface. The vessels are dilated and filled with blood. The capillaries in sections are made out with some difficulty, and only in the tissue close beneath the epidermis. The larger vessels are adjacent to the cartilage and on the outer side. Not only are the arteries and veins dilated, but also all the large lymphatics, which are made out with difficulty in the normal ear, are enormously dilated and may be double the size of the large veins. They usually contain some granular coagulated material and a variable number of cells.

The ear is not the most suitable tissue for the observation and study of the finer details and progress of the changes, owing to the difficulty of the examination of the vessels. The gradual development of the vascular phenomena may best be followed in the mesentery of the frog. In a curarized male the abdomen should be opened on the left side, a loop of the intestine withdrawn, and the mesentery exposed under the microscope on a suitable carrier. Care must be taken to keep the tissue moistened with salt solution and in as natural a condition as possible. Stretching or twisting must be avoided as this will easily interrupt the circulation in the thin-walled veins. It is not necessary to injure the tissue in any way, for the necessary manipulation for exposing the part and keeping it outside the body inflicts sufficient injury to produce all the phenomena. It is probably impossible to observe a normal circulation in a mesentery so treated, as hyperæmia to a certain degree immediately follows the exposure and handling of the intestine. As seen under the microscope, there is a gradually increasing dilatation of the arteries with a more rapid flow in all the vessels. The axial and plasma zone in the large vessels is very evident, and the flow in the capillaries may be so rapid that it is difficult to distinguish the single corpuscles. The red corpuscles in the larger vessels form a red core in the centre and the white corpuscles roll along in the clear space outside of this. The dilatation of the vessels, with increased rapidity of flow, lasts a variable length of time, depending upon the care which has been exercised in exposing the mesentery. All of the phenomena develop more slowly and are more easily studied the greater the care taken to avoid injury.

In a short while the condition changes; the dilatation of the vessels continues, but the rate of flow in all of them is diminished. It is also seen, and this is a point which is often lost sight of, that the relative number of white corpuscles in the vessels is increased. Despite the dilatation of the vessels the rate of flow is diminished, the axial zone disappears, and the corpuscles fill the vessels. The white corpuscles, however, retain their position in the periphery of the stream and accumulate in such numbers that the inner wall of the vessel becomes paved with them. All the corpuscles pass along more slowly, but the white corpuscles much more slowly than the red, so that more accumulate in the vessels. As the process advances, many of the white corpuscles remain stationary and while attached to the wall undergo amœboid movements. Some after remaining for a time are rolled away by the stream, others become permanently fixed. Although this accumulation of leucocytes is more marked in the veins it takes place to some extent in the capillaries also. Very many more are now seen in these vessels than at the beginning of the experiment. If certain of the amœboid leucocytes attached to the veins are watched they may be seen to pass through the wall of the vessel into the tissue outside. A small protoplasmic protrusion is first seen outside the vessel opposite the point of attachment of the cell, and this gradually increases in size, while the part inside diminishes, until the whole corpuscle has passed without. (Plate XXXIV., Fig. 5.) Outside the vessel the active amœboid movements continue and the corpuscle creeps of its own motion through the tissue, although it may also be seen to be moved passively. This process of emigration takes place now with such rapidity that the vessel is soon surrounded by leucocytes which have passed out. It takes place chiefly in the veins and to a much less extent in the capillaries. It is generally considered that it does not take place from the arteries at all, but I have many times found the mural arrangement of leucocytes and active emigration in comparatively large arteries with thick muscular walls, although I have never seen it in the small arteries which immediately supply the capillaries. It cannot be seen to take place in the arteries of the frog's mesentery on direct observation of the circulation, nor have I ever seen any indications of it in preparations of the rabbit's mesentery made at varying intervals after injuries produced in a number of ways. All this time the circulation has become progressively slower, and finally in places, and in the vessels which are distributed to the mesentery itself, it may cease. The vessels now become packed with corpuscles and a to-and-fro movement is often seen in them. The corpuscles themselves seem to lose their outlines and form a solid mass inside the vessels, while the white corpuscles are passing through, and usually some time after this has begun, the red corpuscles also pass through. This process is much more difficult to follow, but single corpuscles may occasionally be seen in the act of emigrating. It may take place from vessels in which the circulation has ceased, and in some cases numbers pass through at a single spot. When the single corpuscles pass through the process seems to take place very much in the same way as in the emigration of the white. A small thin point first protrudes through the wall and the rest of the corpuscle follows.

The same series of changes which take place in the mesentery of the frog can be seen in the mesentery of the mammal, although here a complicated apparatus is necessary in order that the mesentery may be observed under conditions approaching the normal. An excellent way is to kill animals at various times, from minutes to hours, after injury to the mesentery by the injection of irritating substances, and then to make microscopic preparations of the mesentery. The tissue can be instantly killed and hardened, and the actual conditions thus studied much better than during life. The different pictures of the process which are given in this way are extremely satisfactory. All the details of emigration and diapedesis can be studied, all the varieties of leucocytes can be differentiated, and the part each plays can be determined. (Plate XXXIV., Figs. 1, 2, 5.)

For the study of changes which take place in non-vascular tissues the cornea may be chosen. The literature of acute inflammation of the cornea is enormous. It has been the battlefield on which the conflict as to the character and origin of the cells which appear in the tissues in acute inflammation has been fought. The accessibility of the tissue and its simplicity admirably adapt it for this study. The cornea is covered with the conjunctival epithelium. Its tissue is composed of straight fibres of white fibrous tissue which lie in planes, all the fibres of the same plane being parallel. Between the fibres there is a cement substance which stains brown with nitrate of silver. The cells of the cornea, connective-tissue cells, are much branched, flattened antero-posteriorly, and lie in spaces of the same shape between the fibres. All the spaces open into one another and constitute a series of channels through the tissue which communicate with the lymphatics and lymph spaces in the surrounding parts. There is also a series of more definite lymphatic channels around the nerves which communicate with the cell spaces.

When the corneal tissue is injured to a sufficient degree great numbers of new cells are found in it. The character and origin of these new cells were long in dispute, but it may now be regarded as certainly established that in the early phases of the process these new cells are leucocytes which come from the blood by emigration and make their way into the tissue. If the centre of the cornea has been injured either by cauterization or by inoculation with any one of a number of bacteria, the cells will be found in the lymph spaces of the periphery and also around the central injury. In the latter place a great many of them come from the conjunctival secretion, which after injury to the cornea contains numbers of leucocytes. If flat sections of the surrounding sclera be made, the same changes which we have seen to take place in the mesentery will be observed. It is necessary, however, for the injury to be of a certain degree, and those injuries in which the tissue is torn are more apt to be followed by the typical phenomena. Very slight injuries affecting only the conjunctival surface, or even extending to the corneal lamellæ immediately below this, need not produce any but the slightest inflammatory lesions in the cornea proper. The leucocytes may be entirely absent.

It is only within comparatively recent years that we have been able to recognize definitely the varieties of leucocytes and the part which they severally play in inflammation. The distinctions are made in part on the morphology of the nucleus and in part on the character of the granules contained in the protoplasm. In the blood of the rabbit the following varieties of leucocytes are found, following the classification of Brinckerhoff: Amphophiles, 40 to 50 per cent.; lymphocytes, 40 to 50 per cent.; large mononuclears, 5 per cent.; mast cells, 4 per cent.; eosinophiles, 1 per cent. The main difference in the blood of the rabbit, as compared with that of man, is the greater relative number of lymphocytes in the rabbit's blood. The amphophiles in the rabbit correspond in all respects save the character of the granulation with the neutrophiles or polynuclear leucocytes in man. The granules of the amphophiles in the rabbit stain with eosin, but not so intensely as the eosinophiles, and they are much smaller. We shall refer to these cells in the rabbit as amphophiles and in man as neutrophiles. The granules are very much more evident in the amphophiles of the rabbit than in the neutrophiles of man.

The leucocytes which most concern us are the amphophiles or neutrophiles. These usually constitute the majority of the leucocytes in the exudation and in some cases they may be the only ones found. (Plate XXXIV., Fig. 3.) They are the first cells to appear in the inflamed cornea, and when the injury is produced by a chemical agent, no other cells are found in the first eighteen hours. They are actively amœboid and may be found in the tissue a considerable distance from the vessel from which they emigrated. They can be easily recognized both in the tissues and in the vessels and there is less doubt concerning them than in regard to any other of the leucocytes. There is very much more doubt regarding the mononuclear leucocyte. The amphophile leucocyte of the rabbit or the neutrophile of man may be regarded as almost the most distinctive cell in the body. It originates in the bone marrow, and when once formed it is not certain that it undergoes any but degenerative changes. We recognize other cells in part by their morphology, in part by their situation and relations with the tissue, but the amphophile leucocyte is characteristic in all situations. When it is found in the tissues under either normal or pathological conditions, we know it has been brought there by the blood and has reached its present location by emigration from the blood-vessels. The mononuclear leucocytes are much less well known, and their morphological characteristics are less marked. They are found in the blood in much smaller numbers and they certainly may be formed in a number of places. The general tendency seems to be to regard them as endothelial in origin and as such they may be formed in any tissue possessing endothelium, and there is scarcely any tissue in the body in which endothelium does not exist. Their numbers in the blood are not subject to the variation which characterizes the other cells. In the inflamed tissues we know that they certainly in part come from the blood and in hardened preparations they may be found in the act of emigration, but it is infinitely more difficult to see this than it is in the case of the polynuclear leucocytes. They are usually present in small numbers, certainly in much smaller numbers than the other leucocytes, but in rare cases they may constitute the great mass of cells in the exudation. I have seen cases of pneumonia in which all the cells in the alveoli were of this type. It is difficult, however, to distinguish them from the cells derived from proliferation of certain of the epithelial tissues, notably the epithelium lining the alveoli of the lung and the kidney epithelium. In the cornea I have never found them in any number until twenty-four hours after the injury and chiefly around the periphery. They are much less actively amœboid than the polynuclear leucocytes. The same thing is true of the inflamed mesentery. In no experimental inflammation are they found in such great numbers as they are occasionally found in man. These cells can easily

be distinguished from the other varieties of leucocytes by the character of the nucleus and protoplasm. The nucleus is in a single mass and varies in shape, being in different cases round, oblong, or curved. It may have a horseshoe shape with a central constriction, but is never separated into the clumps which are so characteristic of the polynuclear leucocyte. It stains less intensely, and the chromatin is in small masses. The protoplasm is homogeneous or very finely granular and there is no well-defined cell membrane. It seems certain that all of these cells which are found in the cornea reach there from without, but it is not certain that they are all due to emigration. In tissues of more complicated structure it is probable that they are, in part at least, formed from the endothelium of the blood and lymphatic vessels. I have seen in diphtheria the sinuses of a lymph node filled with these cells and have traced their origin to the lining endothelium.

Along with these cells and a little later other cells begin to appear in the inflamed area. These are the lymphoid cells. They are easily distinguished from the other varieties by their small size and their relatively large and brightly stained nucleus. It is also very difficult to explain the origin of these. In the cornea they are never present in any considerable numbers, and then only around the outer edge, but they are found in very great numbers in the surrounding tissue. They are feebly amœboid and their presence in the tissue is to be accounted for rather by their being conveyed passively in the lymph stream than by their own active movement. In all my study of inflamed tissues I have in only two or three instances undoubtedly witnessed their emigration, as shown by cells partly within and partly without a vessel. In the spleen and in the lymph nodes they are not infrequently seen engaged in the walls of the vessels, but whether they are passing from the vessel or into the vessel is uncertain. In the inflamed mesentery of the rabbit they are found in the blood-vessels in considerable numbers after forty-eight hours, but not in such numbers as to explain by this source alone the large numbers of them which may be present in the tissues. In a tissue which contains numerous lymphatics numbers of them are found in these vessels, and it has been supposed that they may reach the inflamed area by this route; but it must be remembered that the direction of the lymph flow is from and not to the inflamed area. The subconjunctival lymphatics around the inflamed cornea may be found filled with them. They may be formed from similar cells in the tissues. A few will always be found in normal tissues in the vicinity of the vessels, and they increase by division, but no one of these means nor the combination of all of them has seemed to me sufficient to account for the great numbers of the cells which may occasionally be found in the late stages of inflammation. Ribbert believes that they are chiefly produced locally by proliferation of the small masses of lymphoid tissue which are frequently found in the tissues, but there are several objections to this view. Such small masses are very infrequent in the mesentery; and in the pleura, where they are found in abundance, there does not seem to be any enlargement accompanying acute inflammations of this structure and of the adjoining lung.

The next leucocyte to be considered is the eosinophile. It is easily distinguished from the other varieties by the nucleus and by the presence of the oblong granules which stain intensely with eosin. In most cases these cells are found in very small numbers. They come from the blood-vessels by emigration and may be seen in the act. I have seen in one specimen an eosinophile cell passing through the wall of a small vein. They are more numerous in the latter stages of inflammation and are extremely variable in number. They appear to be more feebly amœboid than the others. In the cornea I have only occasionally seen them and then never far from the periphery. In one specimen of the mesentery, twenty-four hours after inflammation excited by the injection of one per cent. turpentine, they form the most numerous of the leucocytes in the tissue. In another case considerable numbers of them were found in a specimen made six hours after the injury. In the inflamed tissue around certain animal parasites, notably trichinæ, they may be the only variety of leucocytes found. In a case of echinococcus cyst of the breast in which there was intense inflammation in the surrounding tissue of the mamma they were found in enormous numbers.

The leucocytes in wandering through the tissue in part follow the lymphatic spaces, in part they leave these and make paths for themselves between the fibres. In the cornea, while in the lymph spaces and in the comparatively wide communication between these, they preserve their form to a great extent; when between the fibres they may stretch out into lines which are as thin as the fibrillæ themselves. (Plate XXXIV., Fig. 4.) Few tissues offer a definite bar to their passage. In the cornea I have never found them engaged in the densely hyaline membrane bounding the anterior chamber. Inflammation of the cornea does not involve the anterior chamber except in the case of infectious inflammations combined with necrosis, and when necrotic even this membrane will not prevent their passage. When wandering along the thin spaces of the cornea the separate portions of the nucleus may come together and form a thin rod within the corpuscle, or the widely separated nuclear masses may be connected by a nuclear filament so thin that a high power is necessary to demonstrate it. When wandering in this way the nucleus is drawn to one end of the corpuscle and toward the front end, that is in the direction of motion. In a normal corpuscle there is never a complete separation of the various parts of the nucleus; when this takes place it is evidence of degeneration. They pass through the dense membrana propria below the epithelium of the trachea, and apparently through small spaces in this, for while they are engaged in passing through it they are drawn out into filaments.

The leucocytes, especially the polynuclear forms, may undergo various changes in the tissues after they have left the vessels. These changes are interesting in themselves, and also interesting from the interpretations which have been placed upon them. They may undergo fragmentation in a number of ways. The cells may lose a part of their protoplasm without any apparent degeneration. It is not uncommon to find in the cornea small round masses of protoplasm containing the same oxyphilic granules directly in the wake of the corpuscle. We may find a leucocyte with such small masses almost constricted off. In some cases the fragments contain relatively fewer granules than the main body of the leucocyte. The fragments are not formed by a protrusion of the protoplasmic contents through the cell membrane, but the fragments have a membrane around them like the leucocyte. In the mesentery also these fragments may be found in great numbers. The leucocyte may undergo degenerative fragmentation. This is always combined with degenerative change in the nucleus. In imperfect hardening and staining, and especially in dried specimens of blood, the nucleus appears to be solid and without structure. In reality it is not so, the appearance being due to the abundance and the intense staining of the chromatin. In the fragmenting leucocyte the nucleus is solid and intensely stained. The fragmentation may assume the character of direct cell division. The cell may divide into two parts, each containing a portion of the degenerated nucleus. The whole mass may break up into a number of pieces, each of which may contain a small round particle of the nucleus, or the nuclear fragments may be found together and without any connection with the fragments of the protoplasm. There is no true proliferation of the leucocytes. These fragments, particularly those enclosing particles of chromatin, have been the basis of many of the descriptions of protozoa in the tissues. They form many of the objects which have been described as the parasites of cancers, and are with little doubt some of the things which have been described as parasites in smallpox and vaccine vesicles. I have never seen similar forms of degeneration in the mononu-

EXPLANATION OF PLATE XXXIV.