ing with 67 grains per gallon. All contain magnesium salts, the Champion Spring being first with 193 grains of magnesium bicarbonate per United States gallon. All the springs analyzed according to the more recent methods of examination are found to contain lithium, the Hathorn having 11 grains and the Geyser, Pavilion, and the New Putnam each about nine grains of the bicarbonate to the United States gallon. Most of the other springs contain an appreciable amount of lithium. Iron is always present in all of the waters, from the merest trace in some to 4.62 grains per gallon in the Hamilton, 5.88 grains in the Columbian, and 7 grains in the Putnam springs. All of the springs also contain calcium, while many of them contain the iodide and the bromide of sodium. The Putnam Spring contains the bicarbonate of magnesium. Several well-known springs are not included in the above list, but recent analyses show that they possess the same general characteristics as those of which we have given the analyses.

The Saratoga waters have been recommended in a wide range of disorders and diseases, in many of which they have been found useful, while in others their influence has been pernicious. It can be laid down as an axiom that waters of this strength should not be taken at random; the consumer should invariably give himself the benefit of the advice of a physician of skill and experience before entering upon a course of the waters, either in his own home or at the springs. We cannot in this place enter into a detailed discussion as to the indications and contraindications for the Saratoga waters, but it may be said in a general way that their best application has been found in dyspepsia, engorgement of the liver and portal system, and chronic constipation. The chalybeate waters have been found beneficial as a tonic and reconstructive in general debility, in neurasthenia, and in anæmic states. The springs containing lithia may be counted upon to exercise the same influence upon the protean uric-acid states as is to be expected from the widely advertised lithia waters. Many of the waters are also capable of producing a very appreciable alterative effect when taken for a considerable period of time.

There are three bathing establishments at Saratoga: the Saratoga Baths, recently opened and luxuriously appointed; the Red Spring bathhouse, and the misnamed Magnetic Baths. There is also a bathhouse at the White Sulphur Spring, south of Saratoga Lake. All are well conducted. *James K. Crook.*

SARCOMA.—The term sarcoma is loosely applied to the individual members of a large group of cellular, rapidly proliferating tumors of mesenchymal origin. It is applied more specifically to the members of that subdivision of these tumors in which the tumor cells secrete intercellular substances. The latter are usually small in amount, but they are similar in character to the intercellular substances found in ordinary connective and myxomatous tissues, cartilage, and bone. The tendency is more and more to restrict the name sarcoma to this single class of tumors.

The sarcomata, like other simple tumors, consist of two parts—of the tumor cells which may or may not secrete an intercellular substance, and of a stroma furnished by the tissue in which the tumor grows, in consequence of a physiological demand for nutrition and support made by the tumor cells. The stroma consists of blood-vessels which may or may not be accompanied by a varying number of connective-tissue cells and fibrillæ. The blood-vessels are often of the simplest type and may consist of endothelium only.

The sarcomata may be divided into several groups, according to the production or not of intercellular substances, and the form, arrangement, and differentiation of the cells. These groups can be further subdivided according to the kind of intercellular substance produced, and the size, shape, pigmentation, or other peculiarities of the cells.

The several groups adopted here and the subdivisions under them are as follows:

Group A. Sarcomata Characterized by the Production of an Intercellular Substance.—1. Spindle-cell sarcoma. 2. Myxosarcoma. 3. Chondrosarcoma. 4. Osteosarcoma. 5. Giant-cell sarcoma. 6. Malignant leiomyoma.

Group B. Sarcomata Possessing a Reticulum.—1. Malignant lymphoma. 2. Chloroma. 3. Myeloma.

Group C. Sarcomata having an Alveolar Structure.—1. Melanoma. 2. Alveolar sarcoma.

Group D. Endotheliomata.—1. Hemangioendothelioma. 2. Lymphangioendothelioma. 3. Endothelioma of dura.

Group A. Sarcomata Characterized by the Production of an Intercellular Substance.—The mesenchyma of the embryo gives rise to a series of tissues of which the most closely related are ordinary fibrillar connective tissue, myxomatous tissue, cartilage, and bone. The tumors arising from these tissues, or, in the case of cartilage and bone, from the tissues which produce them, are, in their most actively proliferating types, owing to a lack of differentiation, indistinguishable; but the cells almost always preserve, to some extent at least, the property of differentiating in cell or intercellular substance like the cells of the tissue from which the tumor has arisen. For example, the periosteum gives rise to spindle-cell sarcomata with fibrillar intercellular substance; certain parts of such tumors frequently cease to grow rapidly, the fibrillar intercellular substance increases in amount, and is transformed into a hyaline material (osteoid tissue) in which lime salts may be deposited. In other words, some of the tumor cells have gone far enough in their differentiation to betray the nature and properties of the tissue from which the tumor originated.

It is usually claimed that sarcomata starting from ordinary connective tissue never produce bone, but this may not be a correct assumption. A few sarcomata containing bone have been described as arising in situations where no bone ordinarily exists. They may have arisen from misplaced periosteal tissue, but the simpler explanation is that ordinary connective tissue may give rise to tumors containing bone just as we know it often does under inflammatory conditions, as, for example, in the healing of wounds.

In this group are included those sarcomata which produce intercellular substances, such as the fibrillæ of ordinary connective tissue, the mucus of myxomatous tissue, and the hyaline substances of cartilage and bone. The amount of intercellular substance varies considerably and often is quite small, but even in the most cellular tumors, where mitotic figures are very numerous, proper staining of tissues carefully fixed while perfectly fresh always shows a certain definite and often large amount of intercellular substance.

The tumors of this group are subdivided chiefly according to the character of the intercellular substance produced, to some extent, however, according to the character of the cells. The whole group of tumors is, however, so closely related that the division is largely artificial. Combinations of almost any two or more of the varieties recognized is not at all uncommon. They are really classified in accordance with the amount of differentiation shown by a part or all of the cells. For example, if a spindle-cell sarcoma produces in places a mucoid intercellular substance, it is called a myxosarcoma; if cartilage, a chondrosarcoma; if bone, an osteosarcoma. If, on the other hand, giant cells are present in it, the tumor is called a giant-cell sarcoma.

Sarcomata grow by multiplication of their own cells. They do not infect surrounding tissue cells and cause them to turn into tumor cells. On the other hand, a certain amount of reactive proliferation of normal tissues may take place at the advancing edge of a sarcoma, but the cells preserve their normal characteristics. As a sarcoma enlarges it either simply shoves the neighboring tissue back on all sides by expansive growth, or infiltrates and destroys it. No tissue, not even bone, is able to withstand it.

The various sarcomata have the common characteristics of rapid growth, a tendency to ulceration, to local

return after extirpation, and to early and extensive metastases. The metastases may be local by discontinual peripheral growth, or regional by way of the lymphatics, or general by means of the blood-vessels. As a result of local metastases sarcomata often have a lobulated form. As a result of the frequent extension of sarcomata into blood-vessels, general metastases are common; multiple nodules occur in the lungs, liver, spleen, and bone marrow, and occasionally in other organs. Regional metastases are rare except with certain varieties of sarcoma.

Retrograde changes are frequent in sarcomata, especially fatty degeneration, necrosis, and calcification. With some forms hemorrhage is common and may give rise to pigmentation simulating that present in melanotic sarcomata.

The form of the cells in the different sarcomata can be studied best in teased preparations of fresh or macerated tissues, while the intercellular substances are best demonstrated by means of the aniline blue connective-tissue stain.*

1. *Spindle-Cell Sarcoma.*—Of the sarcomata of which the cells produce an intercellular substance, the most common and typical example is the spindle-cell sarcoma (Fig. 4145). The cells are elongated and terminate at each end in a process which may be long or short. In the swollen centre of the cell is an oval or elongated nucleus; occasionally two or more nuclei are present. When the cells are seen in cross section they look like small round cells. The arrangement of the cells is fairly regular; they overlap each other so that the slender ends of one cell come opposite the middle of the cells adjoining it. The cells tend in a general way to run parallel with the blood-vessels; in this way are formed the bundles of cells which in a mounted section are seen to run in different directions. The bundles of cells may be large, or small and closely interwoven.

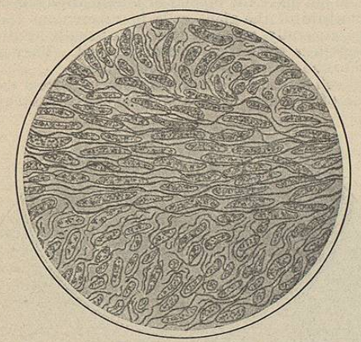

Fig. 4145.—Spindle-Cell Sarcoma showing the Connective-Tissue Fibrillæ Between the Cells.

The cells vary considerably in size and shape in different tumors; they may be large or small, and short and plump with oval nuclei, or very long and slender with rod-shaped nuclei. The two extremes of size are recognized as the large and the small spindle-cell sarcomata.

Mitotic figures vary considerably in number in different tumors and in different parts of the same tumor, but

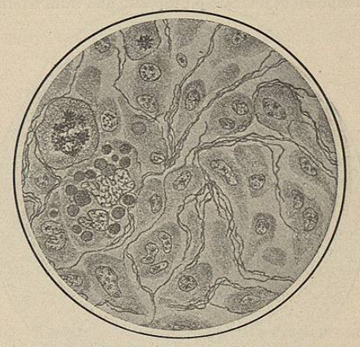

Fig. 4146.—Sarcoma Composed of Large Cells, Round to Spindle in Shape, with Connective-Tissue Fibrillæ Between the Cells. Two mitotic figures of which one is compound. One very large cell contains lobulated nuclei and hyaline droplets. This sarcoma started in the uterus and probably originated in smooth muscle fibres.

usually they are comparatively numerous. The number of them in a given area affords the best means of judging of the rapidity of growth of the tumor.

Running between the cells and in the same direction as their long axes are very delicate connective-tissue fibrillæ, which are produced by the tumor cells. In the more slowly growing sarcomata, and often in certain parts of those which are proliferating rapidly, the fibrillæ are more numerous and tend to unite into coarser fibres.

As a rule, the blood-vessels are very delicate and usually are lined with endothelium only.

All spindle-cell sarcomata do not grow at the same rate of speed. Some contain great numbers of mitotic figures and little intercellular substance; others have fewer proliferating cells and more intercellular fibrillæ. It is not always easy to draw the line between them and the more slowly growing connective-tissue tumors to which they are intimately related. When the cells and fibrillæ are about equal in quantity and the tumor is growing rather slowly, it is called a fibrosarcoma. When the fibrillæ greatly preponderate and the growth is very slow, the tumor is called a fibroma. Names are assigned to but these three rates of speed, and all tumors of this nature are arbitrarily classed under one or another of them.

The spindle-cell sarcoma has its prototype in young connective tissue which it sometimes very closely resembles. I have recently found that young connective-tissue cells of inflammatory origin produce two kinds of fibrillæ—the ordinary delicate wavy fibrillæ which stain blue by the aniline blue connective-tissue stain, and delicate refractile straight fibrillæ which stain intensely red by the same method, provided the staining with acid fuchsin be prolonged for twenty-four hours, and which have about the same relation to the cell protoplasm that the neuroglia fibres have. These red-staining fibrillæ do not stain by Weigert's method for elastic fibres, but can be brought out sharply by a method which has not yet been published. These same fibrillæ occur in spindle-cell sarcomata.

Although the spindle-cell sarcoma is the typical and most common example of the tumors which produce a fibrillar intercellular substance, certain other sarcomata occur in which some or all of the cells may be oval, polymorphous, or even round (Fig. 4146), but they must be carefully distinguished from those tumors in which the cells lie in a reticulum or have an alveolar arrangement.

2. *Myxosarcoma.*—The tissue (Wharton's jelly) of

* *Aniline Blue Connective-tissue Stain.*—This method, slightly modified from the original, is as follows:

1. Fix thin sections (2 to 4 mm. thick) of perfectly fresh tissue in Zenker's fluid for twenty-four hours. Wash in running water twenty-four hours. Dehydrate in ninety-five-per-cent. alcohol.
2. Stain celloidin or paraffin sections in a one-half-per-cent. aqueous solution of acid fuchsin for five minutes.
3. Wash off quickly in water (not over five seconds).
4. Place in a one-per-cent. aqueous solution of phosphomolybdic acid for ten to twenty minutes.
5. Wash off quickly in water (not over five seconds).
6. Stain in the following aniline blue solution five to ten minutes. Aniline blue soluble in water (Grübler), 0.5; orange G (Grübler), 2.0; oxalic acid, 2.0; water, 100.0.
7. Wash very quickly in running water (not over five seconds).
8. Wash in several changes of ninety-five-per-cent. alcohol.
9. Absolute alcohol, xylol, xylol balsam.

Water extracts the acid fuchsin very quickly. Alcohol has little effect on the acid fuchsin but extracts the aniline blue rather quickly.

which the umbilical cord is composed has always been held up as the type of myxomatous tissue. It is usually said to be composed of delicate irregular cells united by protoplasmic processes between which is a fluid or gelatinous ground substance containing mucin. Such a tissue composed of delicate protoplasm and fluid would tear

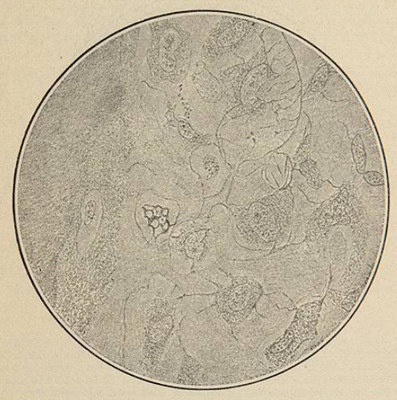

FIG. 4147.—Osteochondrosarcoma. An area where the fibrillar intercellular substance shows partial transformation into the hyaline matrix of cartilage and bone.

with the greatest ease; the umbilical cord is unquestionably rather tough. As a matter of fact, proper staining of the umbilical cord, even in the very smallest embryos, shows that innumerable exceedingly delicate connective-tissue fibrillæ run in parallel strands everywhere between the cells. Myxomatous tissue is, therefore, to be defined as connective tissue in which the individual fibrillæ are more or less separated from each other by a fluid containing an excess of mucin. The ordinary staining methods do not bring out these fibrillæ distinctly. Myxomatous tissue differs from œdematous connective tissue chiefly in the amount of mucin present in the fluid.

A myxosarcoma is to be defined as a sarcoma which produces a fibrillar intercellular substance together with a fluid containing an excess of mucin. The amount of fibrillar material varies with the rapidity of growth of the cells, just as it does in a spindle-cell sarcoma. A pure myxosarcoma is rare; its cells are irregular, more or less stellate, with branching processes. As a rule, only parts of a tumor are myxomatous and the stellate cells grade off into others of the spindle type and the intercellular fibrillæ are closer together and more evident.

3. *Chondrosarcoma.*—The chondrosarcoma is a sarcoma, usually of the spindle-cell type, in which in places the fibrillar intercellular substance has become homogeneous and transformed into a hyaline material having the appearance and chemical properties of cartilage. The change is perfectly analogous to that which takes place under normal conditions in the repair of injuries to cartilage, where the new cartilage is produced by a proliferation of the perichondrium which forms young connective tissue; this is then transformed into cartilage. At the same time the spindle cells change their form and become more or less round or irregular. A chondrosarcoma is, therefore, a sarcoma of which a part of the cells have differentiated far enough to produce cartilage (Fig. 4147).

4. *Osteosarcoma.*—The osteosarcoma is a sarcoma, usually of the spindle-cell type, in which in places the cells have been transformed into bone corpuscles and the intercellular fibrillæ into a homogeneous substance in which lime salts have been deposited (Fig. 4147). This process is analogous to that which takes place in the repair of bone; the periosteum and endosteum produce young connective tissue which is transformed into bone.

If lime salts are not deposited in the osteoid tissue, the tumor is called an osteoid sarcoma. Osteosarcomata usually arise from the periosteum and endosteum.

5. *Giant-Cell Sarcoma.*—It is a question whether or not sarcomata containing giant cells should be put in a class by themselves. Giant cells occur in spindle-cell sarcomata which have no relation with bone (in one case they were present in a primary sarcoma of the left auricle of the heart), they occur in fibrosarcomata, in tumors which grow so slowly and are so benign that they must be regarded as fibromata, and most frequently of all in osteosarcomata. Many writers seek to restrict the term to those tumors which arise from bone, but this seems hardly justifiable. A tumor should be classed by what it contains and itself shows, not by the tissue from which it is supposed to have arisen.

Large cells containing several nuclei, or a large lobulated nucleus, occur in many rapidly growing tumors. These cells are usually, perhaps always, the result of irregular mitoses; that is, the mitotic figure is compound and the nucleus divides into several or even into many nuclei; the nuclei may remain more or less connected together and form a large lobulated nucleus. It is not customary to speak of these cells as giant cells. The term is reserved for cells which contain usually many more nuclei, often a hundred or more; and so far as known these giant cells are not the result of mitoses but of direct division and possibly also of fusion of cells. They have been regarded by many as foreign-body giant cells, but Ribbert looks upon them as attempts at the formation of osteoclasts; that is, they represent on the part of the tumor a certain form of differentiation of the cells. In favor of the foreign-body irritation view is the fact that the protoplasm of these cells usually contains clumps of minute elongated fissures which may have been filled in the fresh state by fat or other crystals. The nuclei do not have the bipolar or mural arrangement so characteristic of the giant cells in tuberculous lesions, but are generally grouped together, usually centrally, but sometimes toward one end of the cell. They never extend to the periphery of the protoplasm.

Giant-cell sarcomata arise most commonly from the endosteum of the long bones and from the periosteum of

FIG. 4148.—Giant-Cell Sarcoma, showing Connective-Tissue Fibrillæ Between the Cells.

the jaw, but they may occur in other organs, as, for instance, the breast, where they are not so exceedingly rare. The naked-eye appearance of them is characteristic. The cut surface is almost always brownish-red over a considerable extent, in consequence of previous

hemorrhages, as a result of which the tumor cells often contain much pigment.

While the cells associated with the giant cells are usually spindle-shaped in type (Fig. 4148), they may be polymorphous or even round, although the latter form is rare. The formation of bone in these tumors is common, but may be absent even where the growth develops from endosteum.

The term *epulis*, applied by the clinician to all tumors growing on the jaw, is sometimes employed clinically as practically synonymous with giant-cell sarcoma, because most tumors of the jaw are of that nature.

6. *Malignant Leiomyoma.*—It has been a much disputed question among pathologists whether or not a sarcoma ever arises from smooth muscle tissue. A number of writers claim to have demonstrated the transformation of a myoma of the uterus into a sarcoma, but each later writer doubts the work of his predecessors, and it has been the tendency of pathologists in general to doubt the conclusions of all of them. It is probable that many of these tumors were of smooth-muscle origin, but perfectly satisfactory proof was not offered.

I have recently studied a tumor of the uterus which seems without much question to be a malignant leiomyoma. It was of the size of a cocoanut and was situated in the posterior wall of the uterus. From its inner side a nodule as large as an orange projected into the uterine cavity. The nodule on section was grayish, homogeneous, rather soft, and friable; it cut and looked like a sarcoma. The main tumor mass was in general of the same appearance, but there were scattered through it, especially at the periphery, areas of a tough fibrous character resembling a myoma. The diagnosis made at the time was "large mixed-cell sarcoma."

Smooth muscle fibres have two sets of fibrillæ: those in the periphery are known as the coarse or border fibrillæ; the others are situated between these and the nucleus, and are known as the fine or "binnen" fibrillæ. It is possible to stain the coarse fibrillæ differentially by means of the aniline blue connective-tissue stain and by other methods, so that they stand out in sharp contrast to other tissues. Benda has recently studied these fibrillæ by means of a modication of Weigert's neuroglia stain. He finds them comparable in many respects to neuroglia fibres and names them myoglia fibres. They are probably a supportive tissue for the smooth muscle fibres, for they pass without break from cell to cell.

The tumor in question would naturally be classed as a large spindle-cell sarcoma, although in some places where the cells are largest they are round in shape. Multinucleated cells also occur and mitotic figures are exceedingly numerous. Yet, in spite of its rapid growth, there is between and around all of the cells an abundant fibrillar intercellular substance which has the staining reactions of ordinary connective tissue. In addition, however, all of the spindle cells over large areas have another set of fibrillæ (Fig. 4149), which stain differentially like the coarse fibrillæ of smooth muscle fibres. These cells differ considerably from smooth muscle fibres; they are much larger and have abundant protoplasm; the nucleus is large and oval in shape; the fibrillæ are usually finer; but every gradation between them and typical smooth muscle cells can be found; in other words, some of the tumor cells tend to differentiate into perfect muscle cells. Where the cells are largest, and oval to round in shape, no differentiated fibrillæ can be demonstrated, although the ordinary intercellular fibrillæ are numerous. The tumor seems unquestionably to be a very cellular, rapidly growing, malignant leiomyoma, which probably developed in a myoma. Some parts of the tumor show invasion of smooth muscle tissue: the tumor cells either press between strands of muscle fibres, or infiltrate them and cause the muscle cells to degenerate.

So far as I know, there is only one source of error in the above diagnosis. Young connective-tissue cells of inflammatory and tumor origin produce, besides the ordinary intercellular fibrillæ with which we are acquainted, a second kind of fibrillæ which stain differentially in the same way as the border fibrillæ of smooth muscle fibres; but the two kinds of cells look very different, and the fibrillæ of connective-tissue origin are usually much finer. Moreover, as the connective-tissue cells differentiate and produce an increased amount of intercellular substance, the red-staining fibrillæ diminish in number. In smooth muscle tissue under the same conditions they increase in number.

FIG. 4149.—Malignant Leiomyoma, showing One Cell in Mitosis and many Differentially-Staining Coarse Fibrillæ Characteristic of Smooth Muscle Cells. The ordinary connective-tissue fibrillæ between the cells are not stained by the method employed and hence do not show.

I have had the opportunity of studying but three other sarcomata of the uterus: two were typical spindle-cell sarcomata derived without doubt from connective tissue; of the third only a small piece projecting into the vagina was obtained. Histologically it closely resembled the most cellular portions of the malignant leiomyoma just described, but no differentially staining fibrillæ could be found in it.

The large amount of ordinary fibrillar intercellular substance in this tumor, in spite of its rapid growth, makes one wonder if it also, as well as the differentially-staining coarse fibrillæ, may not be the product of the cells. Probably the simpler explanation is that the tumor cells, like ordinary smooth muscle fibres, make a demand on adjoining connective tissue for an abundant supply of connective-tissue fibrillæ to surround and support each cell.

GROUP B. SARCOMATA POSSESSING A RETICULUM.—Lymphoid tissue throughout the body, in lymph nodes, spleen, and elsewhere, is composed, aside from blood-vessels, of three different kinds of elements—of a connective-tissue reticulum with the cells which produce it, of endothelial cells which line the reticulum in places, and of lymphocytes (*i.e.*, the different cells of the lymphocyte series) which fill the spaces in the reticulum.

When a tumor develops from these lymphocytes, new blood-vessels and reticulum are formed and there may be more or less proliferation of the endothelial cells, but these are all secondary or reactive processes. The essential part of the tumor is the cells derived from the lymphocytes. They alone give rise to metastases, and, wherever they lodge and proliferate, blood-vessels and reticulum are provided for them.

The lymphocytes of lymphoid tissue are in part undifferentiated lymphocytes such as fill the germinative centres of Flemming, in part the typical differentiated small lymphoid cells such as are met with in the circulation, and in part the more or less differentiated cells, including the plasma cell, between these two extremes of the lymphocyte series.

The undifferentiated lymphocyte corresponds with and is probably identical with the undifferentiated cell of the bone marrow. Dominici has shown that, in the rabbit at least, the undifferentiated lymphocyte in the spleen under the influence of various toxins can give rise to cells

which are identical with the orthobasophilic myelocytes of the bone marrow, and from these cells ordinary polynuclear leucocytes may be produced.

It is evident, therefore, that the tumors arising in lymphoid tissue will not necessarily all show exactly the same type of cell. As a matter of fact, the cells vary considerably. Sometimes they resemble the typical lymphoid cell, sometimes the undifferentiated lymphocyte, sometimes they differ more or less from both.

The normal bone marrow contains undifferentiated cells identical with those in lymphoid tissue. From them develop not only lymphoid and plasma cells, but also the amphophile and other myelocytes. Tumors can evidently arise, therefore, in the bone marrow identical with those originating in lymphoid tissue; but as the cells of the bone marrow under normal conditions undergo much greater differentiation than the cells in ordinary lymphoid tissue, it is not surprising that tumors arise in the bone marrow which are peculiar to that tissue.

This group of tumors arising in lymphoid tissue and in the bone marrow agree in two points: the cells are more or less spherical and are embedded in the meshes of a connective-tissue reticulum. It is difficult to define and classify them exactly, because there is comparatively little that is known positively about them. They unquestionably should be classified according to the differentiation of the chief cell of which they are composed.

The clinical history of this class of cases is always of the greatest importance, and yet even with that, if only material obtained at a surgical operation is available, a final diagnosis may not be justifiable unless the subsequent history also is obtained and in case of death a careful post-mortem examination is made. Various causes can lead to great enlargement of lymph nodes. The difficulty is to know when the enlargement is due to true tumor formation and when to other causes, when the tumor is primary and when secondary.

The inflammatory lesions of the inguinal lymph nodes secondary to gonorrhœa are fairly characteristic and should lead to no trouble in diagnosis, especially with a history of infection. The same is true of many other acute enlargements. The chronic enlargements are more difficult. Some are due to tuberculosis, others to syphilis, and still others to causes not yet fully understood. Hodgkin's disease is a clinical picture which has not a definite pathology. The name is best limited probably to those chronic enlargements of the lymph nodes which at present have no known etiology. Such enlargements are characterized by thickening of the reticulum, the

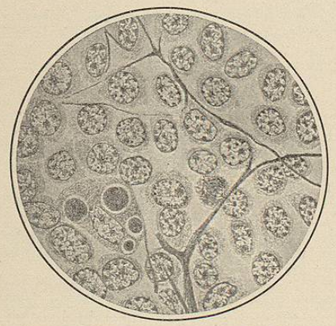

FIG. 4150.—Malignant Lymphoma, showing the Characteristic Reticulum, One Cell in Mitosis, and One Large Phagocytic Cell.

presence of many eosinophiles and of numerous large cells with multiple nuclei or with a large lobulated nucleus. These large cells are probably derived from the endothelial cells which normally line the reticulum in places. The enlarged nodes remain discrete; the sinuses and lymph nodules usually do not disappear.

The most difficult question remaining to be settled in connection with these tumors is their relation to the leukæmias. If the latter, as seems not impossible, should prove to be true tumor formations with metastases growing in the circulating blood because the cells are highly enough differentiated to find the best conditions for their growth there, the relation would be a simple one, and they could readily be classified. If, on the other hand, the leukæmias are simply the expression on the part of the bone marrow of a reaction to toxins or other definite causes, they would have no relation at all to the class of tumors under discussion. The term pseudoleukæmia should probably be given up. The cases diagnosed as such should be included under malignant lymphomata or under the chronic inflammatory processes (Hodgkin's disease).

1. *Malignant Lymphoma.*—The term lymphosarcoma is often used for this class of tumors, but malignant lymphoma is probably better. It is applied to a rapidly growing tumor, of which the actively proliferating cells are of the type of the cells in the lymphocyte series and are embedded in the meshes of a delicate reticulum (Fig. 4150). The small round-cell sarcoma and probably some of the large round-cell sarcomata belong under this same heading. It may be possible later to subdivide this group according to the differentiation of the cells, which are not always of the same character. In the majority of the cases they resemble more or less closely the undifferentiated lymphocyte, but apparently cases occur, although I have seen none, in which the cells are of the type of the differentiated lymphoid cell.

The nuclei of these cells are in general round, although irregular and indented forms are common. They are vesicular in type and contain one to several coarse chromatin granules, but no differentiated nucleolus. Mitotic figures are as a rule numerous. The protoplasm is almost always small in amount, non-granular, but sometimes finely reticular. The cells vary more or less in size in different cases. As a rule they are about as large as the undifferentiated lymphocyte, but occasionally cases occur in which the cells are considerably larger, although otherwise agreeing with them in all respects.

Phagocytic cells are always present in these tumors, so far as my experience goes. They vary greatly in different cases both in size and in number. Often each phagocyte will contain half a dozen or more inclusions. They are unquestionably derived from the endothelial cells lining the reticulum.

Eosinophiles, although generally few in number or altogether absent, occasionally occur in great numbers. In one case at the Boston City Hospital, in a man fifty-five years old, the tumor started just over the symphysis pubis and reached the size of "two fists" in the ten months preceding operation. It extended into the scrotum, along the left vas deferens, and infiltrated the skin. It recurred within a few weeks in the skin covering the dorsum of the penis, in the corpora cavernosa, in the left inguinal lymph nodes, and in the left hypogastrium. The cells were of the type of the undifferentiated lymphocyte. Unquestionably the case was one of rapidly growing malignant lymphoma, and yet polynuclear eosinophiles were present in great numbers everywhere in the tumor, and in places formed one-fourth to one-half of the cells present.

The reticulum is fairly abundant and usually quite delicate, but may sometimes in places be dense and even hyaline.

A malignant lymphoma may arise anywhere where there is lymphoid tissue, but originates most commonly in lymph nodes and in the lymphoid tissue of the pharynx and intestine. Although when the tumor starts in lymph nodes several of them almost always appear to be affected together from the start, it is probable that the growth starts in one node and rapidly spreads to others.

Sometimes the invasion of a lymph node is distinctly visible to the naked eye on section. At other times it can readily be made out on microscopic examination. The normal tissue is rapidly invaded and destroyed, so that

the sinuses and lymph nodules disappear. The tumor cells also early infiltrate the connective, fat, and other tissues outside of the lymph nodes, and sometimes extend into blood-vessels and occlude their lumina.

Metastases are frequent. In the great majority of cases they occur only in lymphatic tissue, especially in other lymph nodes, or in the lymph nodules of the intestine where large prominent nodules may arise. The tumor cells spread to the rest of the body by direct infiltration, by way of the lymphatics, and through the blood-vessels. It is by the last method chiefly that they get to the organs where they become fixed in the capillaries, and proliferate, compress, and destroy the cells between the capillaries. In the larger lymph nodes the metastases take place mostly in the peripheral parts near the capsule, where at first more or less circumscribed nodules are formed.

The gross appearance of a malignant lymphoma is more homogeneous and uniform than that of a lymph node, because there is no division into lymph nodules, sinuses, and trabeculæ. The cut surface is grayish-white and juicy, and the consistence usually soft, but hard malignant lymphomata occur in which the reticulum is coarse. This difference in consistence may occur in different cases or in the same case; if in the same case, the older nodules are the harder, the younger the softer.

2. *Chloroma.*—In its histological structure the chloroma corresponds in all respects to the type of the malignant lymphoma; it is composed of mononucleated lymphocytes embedded in the meshes of a reticulum. Its distinctive and characteristic feature is its color, which may vary from grass green to dirty green. The nature of the color is not known. Certain nodules in a given case may be green, while others are colorless. Von Recklinghausen thinks the color is due to the cells, while Huber and Chiari claim that the color is contained in very fine fat droplets. Against this latter view is the fact that the color is not extracted by alcohol (Dock), although it readily disappears on exposure to air.

In all but one case the bones of the skull were the primary focus affected, and the metastases were chiefly in bone tissue or in the periosteum. Only about twenty cases of the disease have been reported. In most of the cases double or unilateral exophthalmus was one of the earliest symptoms due to the development, behind the eyeball, of tumors which soon became palpable.

3. *Myeloma.*—The myeloma is also closely related to the malignant lymphoma. It consists of small round cells embedded in a delicate reticulum. The cells closely resemble plasma cells in certain respects. The protoplasm is basophilic, and the nuclei, of which there are often two or three in a cell, are more or less excentrically situated. The chief point of difference is that the cells have a very distinct nucleolus, which can be stained differently from the chromatin of the nucleus and which has a clear space around it. The chromatin granules are not so coarse as in a plasma cell.

The tumor affects chiefly the flat bones of the skull, the sternum, ribs, bodies of the vertebræ, less often the bones of the pelvis. It always starts from bone tissue, and metastases occur in other bones but not in other organs. The individual nodules are not sharply limited. The growth causes destruction of bone tissue, so that fractures, as, for example, of the ribs, take place easily. Albuminosuria is a fairly characteristic but not absolutely diagnostic symptom of the disease, as it has been found rarely in certain other conditions.

GROUP C. SARCOMATA HAVING AN ALVEOLAR STRUCTURE.—The structure of these tumors is more or less like that of a carcinoma; they consist of a connective-tissue stroma in the meshes of which the cells are embedded.

In this group belong the melanotic sarcomata of which the origin is now pretty definitely settled, and certain other tumors about which but little definite is known.

1. *Melanoma, Chromatophoroma, Melanosarcoma, Melanotic Sarcoma.*—The melanoma is a sarcoma which owes its distinctive name to its color: in the most characteristic cases this is a very dark brown, but it may be a clear brown, or only a light-brownish tint. The tumor is frequently irregularly pigmented, in some parts brown, in others light-colored, in still others colorless. Sometimes only small areas are colored, so that the pigmentation might easily be overlooked.

According to Ribbert, melanomata occur primarily only in the skin, in the mucous membranes arising from it, in displaced parts of the skin, and in the eye. They

FIG. 4151.—Melanoma of Skin, showing Alveolar Arrangement of Cells with Deep Pigmentation of a Few of Them.

arise from pigmented cells or chromatophores, certain differentiated cells of mesenchymal origin which produce pigment but probably no intercellular substance. These cells occur normally in the choroid and iris of the eye, and in certain situations in the pia and skin. They are also present more or less abundantly in the congenital soft warts or nævi of the skin. As it is from these nævi that melanomata of the skin almost invariably arise, some account of their structure is important. They consist of groups of medium-sized cells having more or less of an alveolar arrangement. The cells are round or irregular in shape and often have short processes. Within the cell groups the pigmentation is usually slight or even wanting, but at the periphery, especially adjoining the epidermis, the cells are usually larger, much more irregular in shape with branching processes, and deeply pigmented. These cells are typical chromatophores; the other cells are to be regarded as young forms produced in excess.

Two types of melanomata occur. In one the cells are more or less round or irregular in type, and are arranged in fairly distinct alveoli (Fig. 4151). This form is spoken of as the alveolar melanoma and is the common type in melanomata arising from the skin. The other form, the spindle-cell melanoma, is much rarer; it is composed of long spindle cells, and occurs most commonly in the eye. It bears a close resemblance, except for its pigmentation, to the ordinary spindle-cell sarcoma, but the vessels run between the bundles of cells instead of in the centre of them. Unless it be demonstrated that these spindle cells produce an intercellular substance, this form of melanoma is best regarded simply as a modification of the ordinary alveolar melanoma; *i.e.*, its groups or alveoli of spindle cells are large and rather indefinitely separated from each other by delicate blood-vessels accompanied by a very slight amount of connective tissue. Rapidly growing carcinomata sometimes show an equally indefinite alveolar arrangement. This view is favored by the fact that all gradations between the two types of growths are said to occur.

It is very important, in the study of the forms of the cells in melanomata, to examine teased fresh specimens, because they cannot be made out nearly so well in stained sections. The cells may be round, irregular, spindle-shaped, or have short or long, simple or branched proc-