esses. The latter forms are more evident in the melanomata of the eye.

The pigmentation is fairly uniform only in the dark-brown tumors. In the others it affects only a part of the cells or a few of them, or may be lacking in whole sections. The cells in the separating strands are usually deeply pigmented. The pigment occurs in the form of brown angular granules and is an essential product of the cells. It is termed melanin, contains no iron, and is probably derived from albumin because it contains sulphur. Melanomata may contain pigment which gives the iron reactions, but this is secondary to hemorrhage which is not infrequent in this class of tumors.

The melanoma is prone to recur after extirpation and to give rise to metastases. This is probably to be explained in part by its tendency to extend along the lymphatics. It usually affects first the neighboring lymph nodes, but soon spreads throughout the body by means of the blood. It develops in the form of nodules of all sizes in all organs, but usually most abundantly in the liver. The color of the metastases may be like the original growth, or darker or lighter. Black and white nodules may occur side by side.

As the melanoma is derived from the chromatophores, Ribbert suggests the term chromatophoroma for them. The only objection to the term is its length, which renders it somewhat undesirable. Melanoma is simpler and calls attention to the important characteristic of the tumor. The terms melanosarcoma and melanotic sarcoma are in good usage, but might be considered to apply also to tumors colored by iron-containing pigments.

2. *Alveolar Sarcoma.*—Under this heading have unquestionably been grouped in the past a variety of tumors of which some at least do not belong here. Many have unquestionably been carcinomata, others endotheliomata. Ribbert has called attention to the fact that melanotic sarcomata are sometimes so slightly pigmented that their real nature might easily be overlooked. Under such conditions they might readily be put into this class. It has been suggested but not proved that alveolar sarcomata may arise from striated muscle cells. For the present this group of tumors must be regarded with suspicion. Many, perhaps all, belong under other titles.

Group D. Endotheliomata.—The endotheliomata form a group of tumors which are very difficult to characterize so that they can be recognized with ease and certainty. In recent years it has been the custom to call almost every tumor which did not fit in readily with the well-recognized tumors an endothelioma. This has been particularly true of certain tumors called cylindromata, which although of various origin (epithelial, mesothelial, and mesenchymal) have the one common characteristic of producing, in some by cell secretion, in others by hyaline transformation of vessel walls, round and cylindrical hyaline masses which are especially noticeable in fresh-teased preparations. At present there is a strong reaction against this tendency.

Endothelial cells normally line blood-vessels and lymph vessels. The cells lining the pericardial, pleural, and peritoneal cavities, and the sac of the tunica vaginalis are now generally recognized as mesothelial in origin and the tumors derived from them are classed with the carcinomata. The space between the dura and the pia is formed by a split in connective tissue, and is lined by connective-tissue cells which become flat and endothelial-like. The tumors arising from these cells are at present classed with the endotheliomata, but further researches may decide that they should be put in a class by themselves.

Endothelial cells possess few characteristics by which they can be recognized with surety; in other words, they do not possess a high degree of morphological differentiation. They are relatively large, thin, flat or curved cells with lightly staining oval nuclei, in which occur usually one or more somewhat coarse chromatin granules but no differentiated acidophilous nucleolus. They line vessels or spaces and are not supposed to secrete an intercellular substance. They are joined to each other at the edges by cement substance along an irregular line, which can be demonstrated in the fresh condition by staining with nitrate of silver. Under certain conditions endothelial cells may become very phagocytic for other cells.

None of these properties is sufficiently marked by itself to characterize with certainty tumors derived from endothelial cells, and yet it is on these more or less characteristic properties that the diagnosis of endothelioma must be based.

The diagnosis in the past has been made largely in two ways: by the process of exclusion and by the demonstration of actual connections between the tumor and blood- or lymph vessels. If a tumor resembled an epithelial growth but originated in a place where epithelium did not normally occur, it was diagnosed as an endothelioma. For example, the cholesteatoma was at one time regarded as a typical example of an endothelioma. The second line of argument used, that a tumor must be an endothelioma because actual connection between vessels or cell masses of the tumor and the blood or lymph vessels of the surrounding tissue can be demonstrated, has been shown by Ribbert to be absolutely untenable. Tumors grow by proliferation of their own cells, not by causing the cells in the tissues around them to multiply and join the tumor mass. Tumors may and often do form connections with surrounding blood- and lymph vessels and with epithelium, but that does not prove that they arose from them. The demonstration of the origin of a tumor from a given cell or tissue is possible only when it is just starting, at a stage when it is rarely or never possible to see it. As a result we are compelled to base our diagnosis on the properties or differentiation of the cells of which the tumor is composed.

Three types of endotheliomata are recognized: one arises from the endothelium of blood-vessels, a second from that of lymph vessels, and the third from the cells lining the dura. The attempt has recently been made to add a fourth, the perithelioma, as a variety of the endothelioma arising from lymph vessels.

1. *Hemangioendothelioma.*—This tumor is derived from the endothelium of blood-vessels and is rare. It grows in the form of narrow or broad anastomosing vessels of a capillary type, which may become filled up with endothelial cells so that solid anastomosing columns of cells are formed. Connective-tissue fibrillæ gradually grow in between the cells, so that the older parts of the tumor resemble more or less closely a spindle-cell sarcoma.

I have recently studied one of these tumors in which all stages of its development could be followed. The primary growth occurred on the back of a boy, sixteen years old, and was followed by three recurrences in the course of the following twenty-one months. Each time the tumor appeared in the form of a group of discrete nodules, from the size of a millet seed to masses 3 or 4 cm. in diameter. The original growth seemed to be attached to the head of a rib, which was resected, but it was not adherent to the skin, and in the recurrences the nodules could always be easily dissected out. The nodules varied from a soft, elastic, almost diffluent to a cartilaginous consistence. On section they varied from reddish to gray; the cut surface was smooth and homogeneous, like a sarcoma.

The earliest appearance of the lesions and the evident source of the recurrences were to be found in the fat and connective tissue outside of the nodules. Here occurred irregular, often long convoluted masses of capillary vessels containing red blood corpuscles and leucocytes, and lined with prominent endothelium. The capillaries ran in the connective tissue often along large blood-vessels and in places invaded fat tissue, gradually causing it to disappear and giving rise to miliary tumor nodules. In all of these small areas and nodules the capillaries were pervious, contained blood, and mitotic figures in endothelial cells were numerous.

In the large, more distinct tumor nodules the appearances were not so simple. Capillaries and larger blood-vessels were very numerous, but there were in addition solid anastomosing columns of cells and a cellular tissue

resembling to some extent young connective tissue or a spindle-cell sarcoma. Both of these were found to arise from the capillary vessels in the following way: Mitoses were very numerous in the larger nodules, not only in the capillary endothelium, but also in the cell columns and in the sarcoma-like tissue. Proliferation of the capillary endothelium often led to occlusion of the lumen and the formation of a mass of cells which often assumed a more or less concentric arrangement. Proliferation of cells beyond the point of occlusion produced anastomosing columns of cells. Hemorrhages and other causes which interfered with the circulation in the young vessels probably also led to the same result.

The second stage in the development of these tumors was, therefore, due to the occlusion of a certain number of capillaries. Continued proliferation of the endothelial cells led necessarily to the formation of clumps and anastomosing columns of cells. At this stage the tumor to some extent resembled a carcinoma, but both the cell masses and the stroma showed differences.

The third stage was due to a still further change. The aniline blue connective-tissue stain showed that the very youngest of the newly formed tumor capillaries quickly become backed by connective-tissue fibrillæ. As the vessels get older the fibrillæ increase in number. In the same way the fibrillæ surround and invade the cell masses formed after the capillaries become occluded. They gradually separate the cell masses so that each individual cell is separated from its neighbor by fibrillæ. But even here small concentrically arranged clumps of cells are often found where rapid proliferation has taken place and separation of the cells has not yet been effected.

Whether or not these endothelial cells produce the fibrillæ, I am not prepared to say. The process probably is analogous to that seen in acute desquamative glomerulo-nephritis where connective-tissue fibrillæ soon extend in between all the desquamated epithelial cells, probably in consequence of a physiological demand for them.

2. *Lymphangioendothelioma.*—This form of endothelioma is derived from the endothelial cells lining lymph vessels and lymph spaces. It usually grows in the form of tube-like or slit-like anastomosing canals, but may form solid anastomosing rows and frequently also concentric masses of cells.

In a case which I have had, the tumor was situated in the lumbar region behind the kidney. It measured over 7 cm. in diameter and was made up entirely of freely anastomosing round, irregular, and slit-like cavities of various size, lined with low, endothelial-like cells (Fig. 4152). In a few areas the lumina of the vessels and the cells to some extent approached a cuboidal form. An occasional endothelial cell in mitosis was found. All of the vessels were backed by a small amount of connective tissue which in places was very œdematous and contained numerous plasma cells.

The term *perithelioma* is applied to a tumor which grows in such a way as to form a sheath around blood-vessels. It is supposed to originate from the endothelial cells (the so-called perithelium) lining the perivascular lymph space. The most typical example is found surrounding the vessels of the brain. If this supposition is true, then a perithelioma is a special form of lymphangioendothelioma.

Sarcomata frequently grow around blood-vessels in such a way as to form a sheath to them, but this manner of growth is rarely or never entirely perithelial. Parts of the tumor or even the greater portion of it may show the picture of an ordinary melanotic, alveolar, or even spindle-cell sarcoma.

The perithelial form of growth is probably largely accidental, and dependent more or less on nutrition. The cells nearest the vessels are best nourished; those farthest away, least so. If necrosis takes place the cells around the vessels are often preserved. The necrotic portions are in time more or less completely absorbed, with the result that the cell-sheathed vessels are but lightly bound together, and in the fresh condition can often be pulled out like the tubules of a normal testicle. It is often possible in a single tumor to trace the entire development of a perithelial growth from a sarcoma of an ordinary type.

It is probable that hemorrhage may act like necrosis in giving rise to the perithelial type of growth.

3. *Endothelioma of the Dura.*—This is the best known of the endotheliomata. It occurs usually as a circumscribed, flat, or more or less hemispherical, occasionally pedunculated tumor. The size varies greatly, but is rarely greater than that of a walnut. The tumor is very lightly attached to the dura by blood-vessels and a slight amount of connective tissue.

The structure of the tumor varies greatly; it may be cellular like a sarcoma or more or less fibrous like a cellular fibroma. The cells may have an alveolar arrangement with the cells often grouped in whorls or the cells may be more or less uniformly distributed in the stroma.

Two cases at the Boston City Hospital illustrate well the two extremes of type. The first measured 5 x 4.5 x 4 cm., and was situated in the right cerebral hemisphere 3 mm. from the longitudinal fissure and 3 mm. posterior

Fig. 4152.—Lymphangioendothelioma, showing Spaces Lined with Flattened Cells and Œdema of the Connective-Tissue Stroma.

to the fissure of Rolando. It was sharply circumscribed, everywhere separated from brain tissue by pia, and presented a cauliflower-like surface. Microscopically it showed dense masses of cells arranged for the most part in whorls, between which ran a stroma consisting of blood-vessels surounded by a small amount of connective tissue, which showed little tendency to extend out between the cells. The nuclei were oval, vesicular, finely granular, with one or more coarse chromatin granules but no differentiated nucleolus. Numerous mitotic figures showed that the tumor was growing rapidly. In places were many hyaline concentrically-layered bodies often containing the faint remains of nuclei.

The second case occurred in the right occipital lobe and measured 8.5 x 6 x 6 cm. It was slightly lobulated and was separated from the brain tissue by the pia. On section it was almost homogeneous in appearance; the surface was grayish, only moderately translucent, and slightly granular. The tissue could be very easily teased apart.

Microscopically the tumor might readily on casual inspection be mistaken for an odd form of spindle-cell sarcoma. Apparently it consisted of numerous spindle and oval nuclei embedded in a fairly abundant connective-tissue stroma. Careful study, especially of sections stained by the aniline blue method, showed that the connective-tissue fibrillæ and the cells were disposed in layers. The layers of fibrillæ ran in parallel planes, which bent and twisted in various directions and often surrounded the blood-vessels. Both surfaces of each layer of fibrillæ were lined by large flat cells, which sometimes piled up two or three cells in thickness. The nuclei were oval and flat, stained lightly, and contained one, sometimes two or more, coarse chromatin granules. No mi-

totic figures could be found. A few concentrically layered cell bodies were present.

Apparently just as the endothelial cells lining blood- and lymph-vessels attempt in tumor formation to form vessels, and, failing in this, give rise to solid columns of cells, so the endothelium lining the dura tends, sometimes at least, in the new growths to which it gives rise to form spaces lined with endothelium. The connective-tissue fibrillæ may be produced, as Ribbert claims, by the endothelial cells, but I prefer to regard them as produced by true connective-tissue cells which grow in with the blood-vessels and extend in between the endothelial cells because there is a physiological demand for them.

F. B. Mallory.

SARSAPARILLA, U. S.—The root of *Smilax medica* Chamisso et Schlechtendal (Mexican, Vera Cruz, or Tampico sarsaparilla), *Smilax ornata* Hooker f. (Jamaica, Central American, Costa Rica, or Lima sarsaparilla), *Smilax papyracea* Duhamel (Brazilian, Para, or Rio Negro sarsaparilla), or a species known commercially as *Honduras* sarsaparilla (fam. *Liliaceæ*). Fruiting specimens just received by the writer from Honduras indicate that the last-mentioned is from *S. grandifolia* Regel. Various other species than those here named have been recorded as yielding sarsaparilla, but it is doubtful if any appreciable amount of the present article of commerce so originates. The genus *Smilax* L. is large, being credited with some two hundred species. Its habits and characters are well illustrated by our ordinary cat-briars, green-briars, or bread-and-butter vines, the green, tough, spiny, tendril-bearing stems of which constitute the principal element in dense thickets of the Eastern United States. Apparently, the Northern species do not possess the medicinal properties of those of the tropics. The aerial stems of the latter grow from excessively long slender rhizomes, which run just underneath the loose forest mould, and send down from each joint a fascicle of from few to many tough, elongated roots, which, dried, constitute the drug sarsaparilla. They are collected at

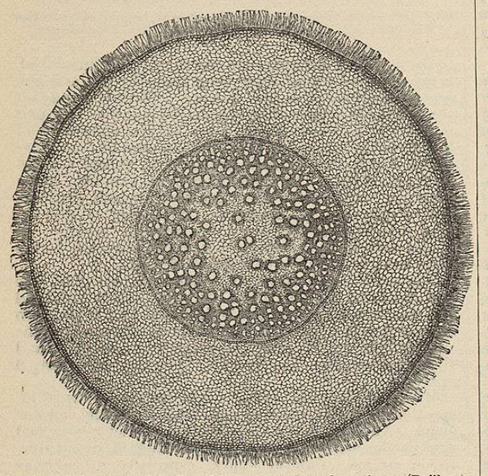

FIG. 4153.—Root of Smilax Officinalis, enlarged section. (Baillon.)

about the close of the rainy season, probably chiefly with the idea of saving labor, since the ground is then soft and the roots are more easily torn out. After being collected and dried, they are packed in various ways, as explained below, these different forms of packing being characteristic, and aiding in identification, although the practice of packing a cheaper article to imitate a more expensive one is not unknown. Other forms of sophistication are not common, though other roots, sticks, and even stones are occasionally found in the interior of the packages.

DESCRIPTION.—Mostly more than a metre (more than a yard) in length, and 4–6 mm. ($\frac{1}{6}$–$\frac{1}{4}$ in.) thick, with few or many fine roots adhering; externally varying from light-gray-brown and smooth, with few deep and sharp wrinkles, to dark- or orange-brown and less smooth, and with more and smaller wrinkles; internally whitish, with a thick, mealy, or sometimes horny cortex, a circular wood-zone and a thick pith; fracture tough; nearly inodorous; taste mucilaginous, somewhat sweetish and bitter, slightly acrid.

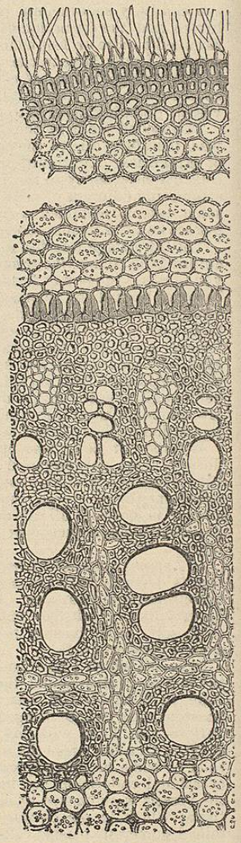

FIG. 4154.—Magnified Section of One-Half Diameter of Root of Smilax Officinalis. (Baillon.)

The thick, woody, knotty rhizome, if present, should be rejected.

As a rule, Honduras and Brazilian sarsaparillas have the cells of the parenchyma more densely crowded with starch grains, so that they are termed "mealy sarsaparillas," the other two being denominated "non-mealy." It is probably due to this excess of starchy contents that the mealy sarsaparilla wrinkle less deeply in their drying, their wrinkles, however, being usually much more numerous than those of the non-mealy varieties.

Honduras Sarsaparilla consists of the roots separated from the rhizomes, folded back and forth to a length of about two feet, and very closely and tightly wound from end to end with one or more of its own roots, the folded ends not cut off, but projecting slightly beyond the winding at either end. These rolls have usually a diameter of about two and a half or three inches. This variety is generally of a rather light brown color. It varies greatly in its tendency to bear rootlets, though as a rule these are not numerous. A transverse section made near to the rhizome shows the diameter almost equally divided between the cortex, wood, and pith. The cells of the endodermis are rather thin-walled, the thickness of the outer and inner walls nearly equal, and the form of the cells nearly square.

Brazilian Sarsaparilla also consists of roots freed from the rhizomes, but it is differently packed. The rolls are very large, a yard or more in length and a foot in diameter. They are rolled with extreme tightness, and closely wrapped with a thin tough vine. The folded ends are cut squarely off and the trimmings enclosed in the centre of the roll next packed, the rolls thus possessing a swollen middle portion. This root is of a very dark-brown color and bears a large number of branching rootlets. It is finely wrinkled. The transverse section shows the woody zone much narrower than the cortical

and the pith large. The cells of the endoderm are radially elongated, with an oblong aperture, and the inner portion of the wall is thicker.

Mexican Sarsaparilla has the roots of each node still attached to a short portion of the hard woody rhizome. They are loosely folded into somewhat flattened bundles, much thicker at one end and loosely tied with a root which passes several times around in an irregularly spiral manner. The root is of a pale drab-brown, often a little shining, almost free from rootlets and bearing but a few wrinkles, which are exceedingly deep and sharp. The transverse section shows very small pith and wood zones, with a very broad cortical layer. The endodermal cells quite closely resemble those of the Brazilian.

Jamaica Sarsaparilla presents two distinct forms. The plant named above is native of Central America, whence the most of our supplies are received. This root is of a dark gray-brown color, rather thin, sharply wrinkled, and very abundantly supplied with branching rootlets. It is always separated from the rhizome and may come either pressed into square bales or tied into rolls with folded ends, like those of the Honduras, but usually thicker, looser, and with a much scantier and looser winding. The other form is known as "native Jamaica" (species of Smilax undetermined), and is the product of plants which have been introduced into the island named. This root is usually much thicker and cleaner looking, and is almost invariably of a bright orange-yellow or orange-red color. It is packed either in bales or in short, thick, lightly tied bundles. The endodermal cells are radially elongated and their walls heavily thickened.

The widest differences of opinion exist as to the relative values of the different varieties of sarsaparilla, and the predominant opinion is not constant, one variety maintaining its position as a favorite for a time, and being then displaced by another. On the whole, Honduras sarsaparilla probably enjoys a wider preference than any other, though the native Jamaican is mostly preferred in Great Britain.

CONSTITUENTS.—Most earnest attempts have been made to find a tangible and useful active principle in sarsaparilla, but with only partial success. From three to fifteen per cent. of starch, according to the variety, a trace of volatile oil, a small amount of resin, pectin, etc., are unimportant. The activity appears to reside in a mixture of three saponin-like bodies, amounting in the specimens examined by Otten to nearly three per cent. Some confusion of ideas has arisen regarding the relations of these substances to one another, on account of the variety of names assigned them by different investigators. Both *parillin* ($C_{26}H_{44}O_{10}$) and *smilasaponin* ($C_{20}H_{32}O_{10}$) have been called "smilacin," and on account of this indefiniteness the last name has been dropped from scientific literature. The third body, *sarsasaponin* ($C_{22}H_{36}O_{10}$), is about three or four times as active as either of the preceding. Like parillin, it is crystallizable, while smilasaponin is not. These constituents are all more or less soluble in water or alcohol, more so upon the application of heat. Either the decoction or a preparation with a warm mixture of alcohol and water well represents the drug. The constituents are fatal to animals, with the general symptoms of poisoning by the sapotoxins.

ACTION AND USE.—Sarsaparilla was first carried to Europe about 1536–45, and first or early employed as a cure for the same disease with which it has been since most generally associated, and for which another smilax, "China," had previously been used. The use in numerous other slow diseases, especially in eruptions and as a "blood purifier" in general, followed, and has continued extensive until the present time. Although now it has been nearly discarded as a serious medicine by physicians, it is still a much-prized popular remedy, and is extensively used, the world over, for syphilitic and scrofulous diseases. Its reputation is doubtless greatly and unduly enhanced by the enormous popular advertising of numerous proprietary articles bearing its name, but in reality quite different substances. On the other hand, there can be no doubt that the judicious use of sarsaparilla by physicians should be extended. The valuable depurative effects of the saponins, not only by promoting excretion by the intestines, but through most other channels, requires no argument, and the timely use of a laxative dose of sarsaparilla, perhaps at the soda fountain—if only a genuine article could be there expected,—may well prevent the necessity for more violent treatment later on. The dose of any preparation should represent from 4 to 8 gm. (℥i. to ij.). The Pharmacopœia provides a fluid extract; a compound decoction of ten-per-cent. strength, with two per cent. each of sassafras, guaiac wood, and liquorice root, and one per cent. of mezereum; a compound fluid extract of seventy-five-per-cent. strength, with twelve per cent. of liquorice root, ten per cent. each of sassafras and glycerin, and three per cent. of mezereum.

ALLIED PRODUCT.—China root, from *Smilax China* L., in large, hard, jalap-like tubers, is used in the East for the same purposes as sarsaparilla.

Henry H. Rusby.

SARSAPARILLA, FALSE. (*Aralia medicaulis* L.) See *Araliaceæ*.

SASSAFRAS, U. S. P.—*Sassafras bark.* The dried bark of the root of *Sassafras Sassafras* (L.) Karsten. (*S. variifolius* [Salisb.] Kuntze—fam. *Lauraceæ*). Although all parts of the sassafras tree are aromatic, the bark of the root is selected for official purposes because its aromatic properties differ in kind from those of the leaves and branches, and are far stronger than the similar properties of the bark of the trunk and the wood of the root and trunk. The British Pharmacopœia makes the root,

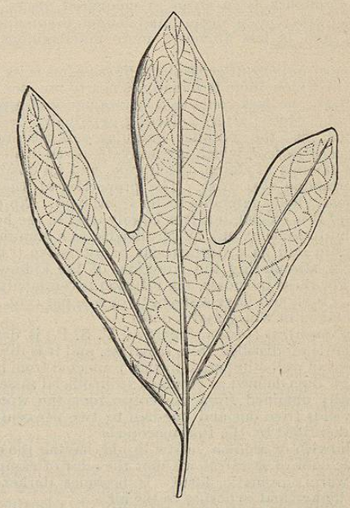

FIG. 4155.—One of the Three-Lobed Leaves of Sassafras. (Baillon.)

the German Pharmacopœia the wood of the root, official, while certain others include, or even specify, the wood of the trunk or at least of its lower portion. There can be no question that the official article of the United States Pharmacopœia is very superior to any other part of the plant. The sassafras tree grows very abundantly in light soil and exposed or partly exposed situations from eastern Canada southward, being collected chiefly in the coast region. It occasionally reaches a height of seventy feet or more and a trunk diameter of upward of three feet, though usually its height is from twenty-five to