ADENO-CARCINOMA. See *Carcinoma.*

ADENO-CYSTOMA. See *Cystoma.*

ADENOID VEGETATIONS. See *Tonsils, Pharyngeal.*

ADENOMA.—Adenoma is the term applied to a new growth originating in glandular epithelium and corresponding in histological structure with the general type of gland tissue.

Every new formation of glandular tissue, every glandular hyperplasia, cannot be regarded as an adenoma, and sometimes it is impossible to say whether an apparent growth is a simple hyperplasia or a tumor. A gland which is increased in size in consequence of excessive nutrition and function cannot be called an adenoma, but must be considered a hyperplasia.

In the same way must be considered those formations in mucous membranes which frequently develop in consequence of chronic inflammation and take the form of tumors. These are local new formations which project above the surface in the form of polypi or papillary masses. The new growth commences in the connective tissue, and the epithelium also takes part in that, by the increase of the surface, the covering epithelium also must increase. If there are glands present their ducts are usually obstructed, and cysts are formed with papillary projections within them. This must be considered simply as a growth due to chronic irritation, and as entirely distinct from the true glandular polyp of the mucous membranes in which a formation of new glands actually occurs. Clinically, these can usually be distinguished, for the simple polyp disappears when its cause, chronic irritation, disappears.

Etiology.—The causation of adenomata is obscure, though probably no more so than that of new growths in general.

In some forms congenital misplacement of tissue elements appears to play an important part. Thus in the kidney, adenomata sometimes are found which correspond in structure to the adrenal. These, as pointed out by Grawitz, develop from aberrant remnants of the adrenal embedded in the kidney substance. This is also true of adenomata corresponding to the structure of the mamma occasionally seen in the axilla, and of the rather unusual substernal tumors in which a tissue similar to that of the thyroid body is found. Here it is probable that the theory of embryonic remains of Cohnheim gives the true explanation: the tumor in each of these instances develops from embryonic fragments which become separated from the gland in its development. Although in certain locations, as the stomach and rectum, the adenomata appear to bear out Virchow's irritation theory, in other locations they offer it no support at all.

The parasitic theory receives absolutely no support from the adenomata, for it is impossible to conceive of a vegetable or an animal parasite causing the reproduction of definite gland tubules.

Varieties and Structure.—The appearance of adenomata varies greatly with their location. Naturally, any particular cell or arrangement of cells cannot be described as peculiar to this tumor, any more than any type of cell can be regarded as characteristic of all physiological glandular structures. The adenomata differ from one another in structure as much as the structure of the liver differs from that of the lachrymal gland.

In the stomach, intestine, and uterus, in a general way, the epithelial cells are arranged as tubular acini with a central lumen, the cells generally occurring in one layer, though there may be more. The acini are separated from one another by connective tissue in which the blood-vessels and lymphatics are borne. Why the cells in their growth should grow as tubules instead of breaking through the basement membrane and forming atypical groups of epithelial cells, as is seen in the form known as adeno-carcinoma, is difficult of explanation. It is probable that the inherent tendency thus to develop is not early influenced by their altered environment. That they do not break through and grow as carcinoma is frequently seen in some large and rapidly growing adenomata. The cells lining the tubules may be columnar or cuboidal, according to the gland from which the tumor develops.

In addition to the tubular form there is an uncommon variety, the racemose adenomata, in which the appearance is that of a complicated gland structure with closely aggregated acini of circular outline containing columnar, cuboidal, or polyhedral cells.

Then, again, in the liver, kidney, and adrenal occur adenomata resembling more or less closely the normal structure of those organs.

As in any other epithelial tumor, the relation between the epithelial cells and the connective tissue varies. When the development of the connective tissue is excessive, far beyond that of the normal gland, it must receive some recognition in naming the tumor, for it is as truly new formed as is the epithelial portion: in such cases it is called an adeno-fibroma. When this connective tissue is especially abundant in cells and represents an embryonic tissue, the term adeno-sarcoma is used. In the ovary occurs an adenoma in which the acini line cyst cavities. This is termed an adeno-cystoma.

Adenomata, as far as known, do not contribute to the body metabolism. That there is a partial preservation of function is occasionally seen. In the adenoma of the liver sometimes a biliary pigmentation occurs; in the adenoma of the breast there may be a secretion of milk-like fluid; in the adenoma of the intestine the tubules may contain mucus; in the adenoma of the thyroid colloid material may collect. But these substances remain in the tubules in which they are formed, and take no part in the general metabolism.

Secondary Changes.—All forms of degeneration are common in adenomata. Hyaline transformation may give the tumor an appearance justifying the term "cylindroma." This, however, is rare. Myxomatous and calcareous degenerations occasionally occur. Cystic change may result from gradual dilatation of the glandular acini. Hemorrhages are common, and on free surfaces ulceration is frequent.

The most important change, however, is a carcinomatous transformation. This is especially common in the stomach, intestine, and uterus. The proliferation of the epithelial cells becomes excessive; the acini become more abundant and irregular; the cells depart from their tubular arrangement and grow as solid epithelial masses outside the acini, forming an adeno-carcinoma, or, as Ziegler named it, *adenoma destruens*. The growth may eventually become purely carcinomatous, but it usually retains more or less its adenomatous type.

General Character.—The rapidity of growth of an adenoma differs in various parts of the body in which it has its seat, and the same holds true for its malignancy. There are few which can be considered as strictly benign tumors. The pure adenoma seen in the liver may form metastases in the spleen and less frequently elsewhere. Fatal metastases from adenomata of the thyroid have been reported. In the sweat, sebaceous, and lachrymal glands the tumor usually grows slowly, remains local, and may be considered benign. In some locations, although adenomata never produce metastases, they may endanger life by their size, as in the ovary; or may obstruct important canals, as in the intestine; or may cause great disfigurement, as displacement of the eye in adenoma of the lachrymal gland. The general health may also be influenced by interference with the normal function of the organ in which they are located, or in consequence of ulceration and hemorrhage. There are few tumors more malignant than the adenomata of the intestinal tract. They extend rapidly, infiltrating all coats of the intestine, and frequently produce metastases in the liver. Their malignancy does not always depend on carcinomatous transformation, for some of the most destructive tumors of this canal are pure adenomata.

As regards the terms Malignant Adenoma and Adeno carcinoma, it seems best to use the former in designating those growths in which, although there is extensive infil-

tration of surrounding tissue and even the formation of metastases, the tumor still retains its glandular type; and to use the term Adeno-carcinoma for those forms in which

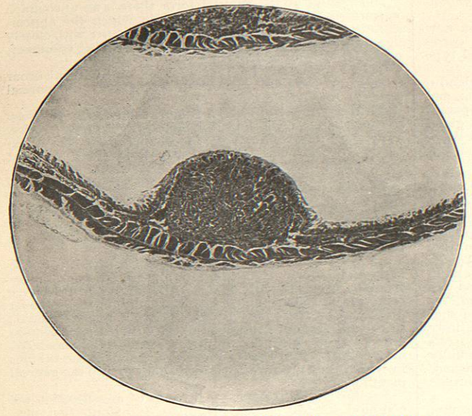

FIG. 36.—Benign Adenoma of Small Intestine. × 10 diameters.

the cells depart from the tubular arrangement with the formation of distinct cancerous areas.

The principal locations in which adenomata may occur and brief descriptions of their characteristics dependent on location and origin are given below:

SKIN.

Adenomata of the skin are rare. They may develop from the sebaceous or from the coil glands. They grow slowly and are practically always benign. Adenomata of sweat glands are found in various parts of the body, but principally on the face, where they are of a dirty grayish-white color with nodular surface. Histologically, coils of dilated ducts are seen, from which degenerated epithelium can be squeezed. Campiniri (1895) describes cystic and carcinomatous changes in such tumors. Adenomata of sebaceous glands appear principally on the face and are usually of congenital origin. They appear as small, roundish, convex papules, of bright color, and in old people are often associated with fibromata.

Whitney has described an adenoma of sebaceous-gland origin which was the size of an orange and contained large cavities filled with a material resembling butter in its color, consistence, and general appearance. (Consult also the special article on *Adenoma of the Skin.*)

MUCOUS MEMBRANES.

Mouth.—Adenoma of the mucous glands of the mouth is very rare. It occurs as isolated nodes and in some cases gives rise to macrocheilia. Adenomata of the salivary glands have been reported.

Larynx and Bronchi.—A few cases have been reported of benign adenomata arising from the mucous glands of these organs. Eber (1896) has reported several cases in the bronchi of sheep. They occur as irregular nodular growths.

Stomach and Intestine.—Small, apparently benign adenomata are sometimes seen. The malignant adenomata and the adeno-carcinomata are the most important forms. They start as soft nodular growths which break down readily and ulcerate. They infiltrate all coats and may cause perforation. Metastases in the liver may occur, and there is sometimes a direct extension to adjacent organs, as from stomach to pancreas. In the large intestine, of all forms of new growth, this tumor is the most common cause of chronic intestinal obstruction. Histologically, they may be made up of dilated, irregularly branching tubules presenting a single layer of cylindrical epithelium—in the stomach originating from the gastric tubules, in the intestine from the glands of Lieberkühn; or in addition to this structure there may be irregular solid masses of epithelium, the result of great proliferation of epithelial cells and destruction of the basement membrane.

In the large intestine the locations, in order of frequency, are the rectum, the sigmoid, splenic and hepatic flexures of the colon, and the cæcum.

In the small intestine adenoma is occasionally found in the duodenum at the papilla marking the orifice of the bile duct.

Vulva.—Benign adenomata arising from the glands of Bartholini have been reported. Kelly describes an adeno-carcinoma, as large as an orange, of the vulvo-vaginal glands.

Urinary Bladder.—Adenomata of this organ are rare. They may be sessile or pedunculated, smooth or lobular, benign or malignant. It is not easy to explain their origin.

Uterus.—Adenoma originates generally in the body of the uterus, but occasionally in the cervix. It may rapidly infiltrate the myometrium and may produce nodules on the peritoneal surface. It has the usual glandular structure and a small amount of fibrous stroma. Carcinomatous areas may develop.

Occasionally a benign polypoid adenoma may be seen, but it is often difficult to distinguish this from a hyperplastic glandular endometritis.

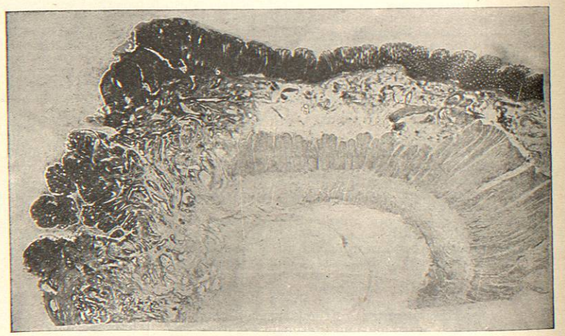

FIG. 37.—Malignant Adenoma of Rectum. × 10 diameters.

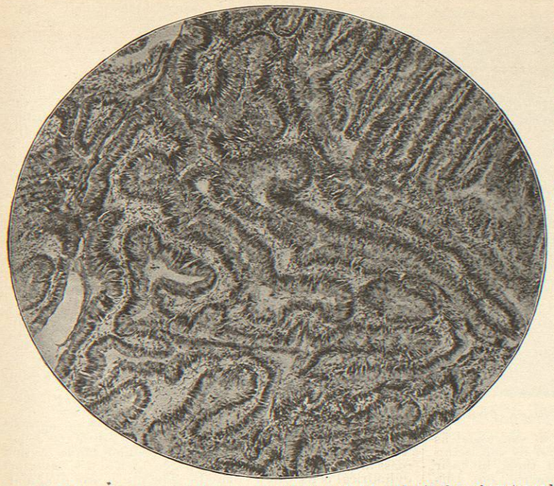

FIG. 38.—Malignant Adenoma of Rectum. Greatly magnified in order to show character and arrangement of the newly formed glands.

Diffuse benign adeno-myomata of the uterus have been carefully described by von Recklinghausen and Cullen.

ADENOMA IN SOLID VISCERA.

Liver.—Adenomata of this organ are rare. They may occur in the normal or in the cirrhotic liver, and appear as small, grayish-white, reddish, or brown miliary solitary or multiple areas. They are made up of tortuous, branching, gland-like tubules of newly formed trabeculæ of liver cells, not arranged as typical liver lobules. The cells are large, pale, and finely granular. They arise from proliferation either of liver cells or of the cells of the bile capillaries. The larger ones have a distinct capsule. Some writers believe that they may become carcinomatous.

Another and rare form is the adeno-cystoma, which is made up of cysts containing a colorless fluid, the walls of the cysts being covered by glandular epithelium. This form probably originates from the bile ducts.

Kidney.—Congenital adenoma, struma aberrata suprarenalis.—As shown by Grawitz, this tumor develops from fragments of the adrenal body which in the development of the kidney become incorporated in its substance. The tumor is small, grayish, and generally just beneath the capsule. Histologically, it consists of large pale epithelial cells arranged in tubules similar to those of the cortical portion of the adrenal. The cells are filled with fat granules. Active proliferation may occur with tendency to malignancy. The observations of Askanazy and Lubarsh indicate that malignant tumors resembling carcinomata may develop from these growths.

Adenomata arising from renal tubules are rare. They originate in the convoluted tubules, and appear as very small nodular masses, though they sometimes may reach a diameter of 3 to 4 cm. They are distinctly encapsulated. The cells may be cuboidal or may become cylindrical, and are arranged in the form of single tubules; the glomeruli and different types of tubules are never reproduced.

A *papilliferous cystic adenoma*, a small tumor with fibrous capsule in which the lining epithelium is elevated in a papillomatous manner, is occasionally seen.

Adrenal.—Adenoma of adrenal, or struma lipomatosa suprarenalis of Virchow, generally develops from the cortex as an irregular nodular growth, yellowish or pale brown in color. It may remain small or may completely destroy the organ, sometimes attaining a very large size. The cells resemble those of the normal gland in structure, but are large, pale, and granular, as though filled with fine fat granules.

Breast.—Many tumors of the breast combined with the formation of cysts have been described under the name of adenoma. In such cases the tumor is generally a fibroma or a sar-

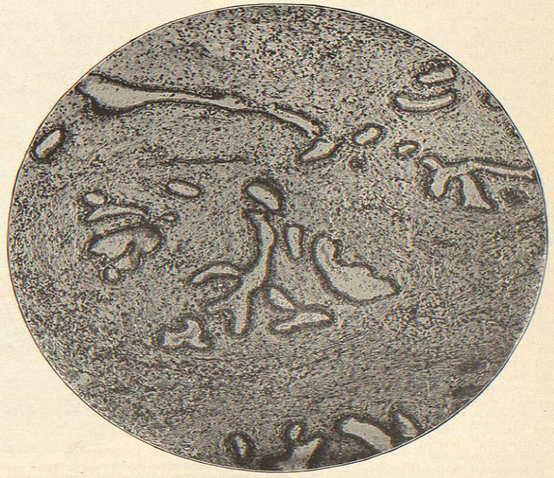

FIG. 39.—Fibro-Adenoma of Mammary Glands.

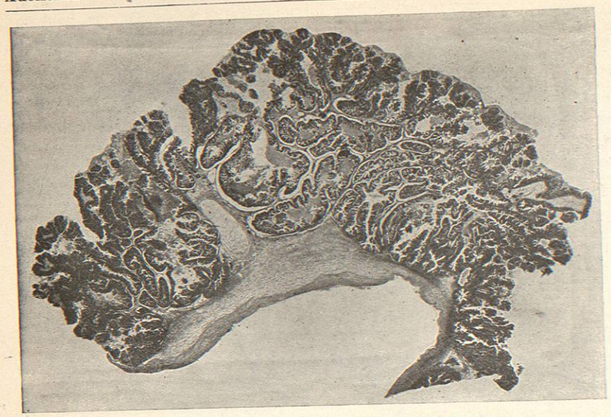

FIG. 40.—Papillary Adeno-Cystoma of Ovary. × 10 diameters.

coma, and has grown into the ducts of the gland as papillary projections. These are covered by the lining epithelium, which they push ahead of them in their growth, and which increases in consequence; but this is only secondary, and these tumors should be considered as connective-tissue formations.

A diffuse enlargement of the breast due to uniform increase in the glandular elements has occasionally been described under the name of diffuse adenoma. This condition is bilateral, usually occurs about the time of puberty, and, strictly speaking, is a hyperplasia and not a new growth.

The *true adenoma* is unilateral, definitely circumscribed, and encapsulated. It usually occurs in young women, starting as small nodes in the upper or outer quadrant of the gland. It becomes round or oval in shape and sometimes grows to considerable size, though usually small. On section it is uniformly smooth, grayish white, and quite firm, though occasionally it is soft and slightly nodular.

Histologically, it may be composed of acini or of ducts lined by cylindrical epithelium. The stroma is fibrous and varies greatly in character and amount, but is looser and more cellular than that of the normal gland. According to the character of the interglandular tissue, it may be an adeno-fibroma, adeno-myxoma, adeno-sarcoma, etc.

Adeno-carcinoma is generally considered to be an unusual form of breast tumor. Halsted (1898), however, reports five occurring in a series of one hundred and fifty breast cancers. According to Halsted's observations, these growths differ from ordinary cancer of the breast in that they are softer, more pedunculated, and discharge a peculiar serous fluid when ulcerated. Histologically, they are composed of very large tubes lined by epithelium many layers deep. In three of Halsted's cases the growth was pure adenoma (malignant adenoma); in the others carcinomatous areas were present. Metastases in the axillary lymph nodes were found in none.

Ovary.—The multilocular cystadenoma is the commonest tumor of the ovary, and the one usually attaining the greatest size. It may be small or it may weigh a hundred pounds or more. It is a benign tumor and never produces metastases. The surface may have no epithelium, or it may have a single layer of flat epithelial cells. The numerous cysts of varying size which make up the mass are lined on their inner surface by a single layer of cylindrical cells, often ciliated. The nuclei are oval and

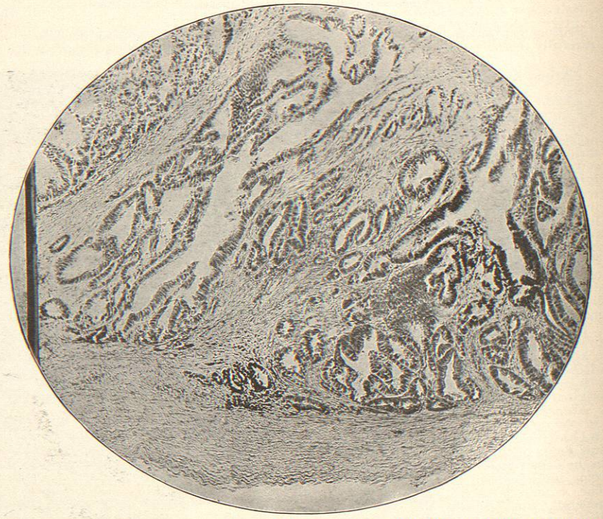

FIG. 41.—Papillary Adeno-Cystoma of Ovary. More strongly magnified than Fig. 40, in order to show cyst wall; papillary ingrowths of connective tissue; epithelium lining papillary projections. As seen in cross section this epithelial structure gives the appearance of a glandular growth.

placed near the basement membrane. Some of the cells may be swollen and filled with clear contents, giving them the appearance of goblet cells. The contained fluid is thick, viscid, sometimes jelly-like, and may be colorless, or, if there has been hemorrhage, yellowish or reddish brown. This fluid is formed by secretion from the epithelial cells, by the transudation of serum from the blood-vessels, and by the degeneration of the epithelial cells. The most important chemical substance in the fluid is pseudomucin, a true secretion of the newly formed epithelial cells. It does not occur in the normal ovary, in dropsical Graafian follicles, or in the parovarium.

Calcification or necrosis of the cyst wall may occur as secondary changes. Both are unusual.

The *papilliferous adeno-cystoma* is characterized by an ingrowth into the cyst of a papilliferous connective tissue covered with epithelium. On cross section the appearance is that of gland tubules. The papillary growths may be prominent, or they may appear simply as flat excrescences on the surface of the cysts. The epithelium is similar in character to that in the multilocular adeno-cystomata. This tumor is not malignant in the ordinary sense; but after rupture of the cysts a local growth on the neighboring peritoneum may occur.

These growths are supposed to originate from the epithelium of mature or residual embryonic follicles or from the germinal epithelium of the ovary. Pflüger has pointed out the glandular structure of the ovary, and Spiegelberg and Langhans have shown in the ovary, even after birth, residues of its embryonic glandular structure. Doran, as a result of his investigations, believed that the tumor might originate in childhood or even in the intrauterine period. Williams states that the papillary adeno-cystomata originate from the epithelium on the surface of the ovary or from that of the Graafian follicles, or from both.

Adeno-carcinoma of the ovary may originate in the ovary, may develop in a papilliferous adeno-cystoma, or may be secondary to a similar growth in the uterus.

Thyroid.—Aside from the hyperplastic changes associated with the condition known as goitre, circumscribed adenomatous tumors of the thyroid occur. These appear as soft nodular growths composed of glandular tubules lined by tall cylindrical epithelium. Within these tubules papillary growths sometimes appear (adenoma papilliferum). Within the tubules is seen the colloid material characteristic of the normal thyroid. Although this tumor is one of the purest types of adenoma, it may produce metastases. It may also by direct extension invade the structure of the larynx.

Testicle.—The form of tumor as it occurs in the testicle is generally known as cystadenoma. It may occur in the child or in the adult. It is attributed by some writers to error in development. Two forms are recognized. In one the tubules are lined by cylindrical cells which sometimes have cilia, their contents being a clear or blood-tinged slimy fluid; in the other the epithelium is stratified and the contents a greasy substance with many fatty epithelial cells. The growth usually starts in the testicle and may attain a large size. Instances of carcinomatous changes have been reported.

Prostate.—The tumor usually occurs in this organ as an adeno-carcinoma and is rare. It appears as soft, nodular masses which project into the urethra or neck of the bladder and invade surrounding tissues. Ulceration is frequent, and when it occurs is accompanied by copious hemorrhage.

Pituitary Body.—Adenomata of this structure are rare, but are occasionally reported in connection with cases of acromegaly. They may be as large as a pigeon's or hen's egg; may protrude from the sella turcica, press on the brain, and extend even into the ventricles. Histologically, they are made up of large, tortuous, sometimes branching tubes lined by epithelial cells.

Pancreas.—Adenomata of this gland are not common. They are generally of the racemose type. Cesaris-Demel (1895) reports a distinctly encapsulated adenoma the size of a dove's egg in an atrophied pancreas. The cells were irregular and primitive, occurring in one and sometimes in several layers, generally arranged in alveoli.

Lachrymal Gland.—Adenomata of this gland are not very common. They generally occur in persons of advanced age. By pressure they may interfere seriously with the movements of the eye. They do not tend to become malignant and are only troublesome on account of their size. Adeno-carcinoma has been reported, but is very rare.

Pineal Gland.—The occurrence of adenomata of this body is occasionally referred to in the literature.

Richard Mills Pearce.

ADENOMA OF THE SKIN.—Adenomatous proliferation of the cutaneous glands is an extremely rare occurrence, and it is only within a comparatively recent period that the condition has been recognized. Hypertrophy of the skin glands, on the other hand, is a concomitant of many chronic local disturbances of nutrition, and doubtless in some of the cases recorded as adenoma there has been confusion between this condition and hypertrophy. The considerations involved in the differentiation of hypertrophy and adenoma have been discussed in the preceding article.

Adenomata of the skin naturally fall into two classes: adenoma of the sebaceous glands (*adenoma sebaceum*), and adenoma of the sudoriparous glands (*adenoma sudoriparum*).

ADENOMA SEBACEUM.—(Synonyms: *Végétation vasculaire* [Rayer]; *Nævi vasculaires et papillaires* [Vidal]; Adenoma of the sebaceous glands; Steatadenoma; German, *Talgdrüsenadenom;* French, *Adénome sébacé.*)

The earliest recorded cases of the disease are found in the writings of Rayer and of Addison and Gull, who, however, failed to interpret correctly the anatomical condition, which Balzer was the first to recognize, though Balzer's case, curiously enough, has been shown by later investigators to be one of acanthoma adenoides cysticum. Cases have since been described by Hallopeau and Vidal in France, Mackenzie, Pringle, Jamieson, and Crocker in England, and Caspary and Boeck in Germany. The only case recorded in America has been described by the present writer.

The disease manifests itself in the form of small multiple benign tumors, which may be distributed generally on the face, but occur most frequently at the sides of the nose. Their distribution is usually fairly symmetrical, but in Jamieson's and one of Crocker's cases they were limited to one side of the face, and in my own case the lesion was in the form of a linear patch on the forehead. The lesions in some cases were present at birth or appeared in infancy; but a more active growth, as to number and size of the tumors, has been noted at the time of puberty. In Caspary's case and in my own they did not appear until the seventeenth and the nineteenth year respectively. The individual growths seldom undergo any change after they have attained their development, though involution of a few of the nodules with resulting faint cicatrices has been noted.

The little tumors vary in size from 1 to 5 mm., are usually round and convex in shape, and the epidermis over them may be smooth or have a rough and somewhat warty appearance. Their color may be that of the normal skin, or they may have a brownish or even bright red hue. The color depends greatly on the presence or absence of telangiectases, which often appear as fine lines ramifying over their surface, and in some cases may form so striking a part of the tumor as to give the whole the appearance of a vascular nævus. In Vidal's case and in mine there was cystic degeneration of a part of the tumors, giving the appearance of small yellow nodules from which on incision a drop of inspissated sebaceous matter could be squeezed. Some importance has been attached to the fact that in many of the cases there were other striking abnormalities of the skin: warts, pigmented and hairy nævi, and small pendulous fibromata indicating a congenital tendency to malformations of the skin. It is probably only a coincidence that