

may almost be regarded as the rule. The frequency of metastases by blood-vessels in carcinoma of the intestinal canal is probably to be explained by the presence, in the latter situation, of numerous and thin-walled veins, which offer less resistance to the extension of the tumor into them. Where the metastases take place depends upon the distribution of the blood-vessels coming from the part. The metastases transported, by way of the blood channels, from the primary tumors of the intestinal canal, are found in the liver, while those coming from tumors in other parts of the body are found in the lungs. There are certain exceptions to this because the tumor emboli may pass like other emboli in the direction opposite to that of the blood current. Thus metastases may be found in the liver secondary to carcinoma of the lung, or in the kidney secondary to carcinoma of the liver. In these cases the emboli are probably larger and are carried by the force of gravity in the reverse direction to that of the blood stream. Very interesting combinations are often found of metastases by both blood and lymph circulation. Thus I have seen in carcinoma of the uterus metastases in the post-mesenteric lymph nodes, and from these a growth of the tumor into the thoracic duct, converting this into a large carcinomatous cord which extended into the subclavian vein. There were numerous very minute metastases in the lung simulating miliary tubercles, and from these extension had taken place into the subpleural lymphatics, which were actually injected with the tumor masses, and into the bronchial nodes. The metastases by way of the blood-vessels may be single or so numerous as to simulate a case of acute miliary tuberculosis. In such cases the condition is spoken of as a general carcinomatosis.

Extension of the tumor may also take place at various places on the surface, due to the implantation of masses of a tumor along an adjoining surface (Plate XX, Fig. 4). We find examples of this in the appearance of numerous nodules on the surface of the peritoneum in carcinoma of the ovary which extends to the peritoneum. Such metastases are most apt to be found in those situa-

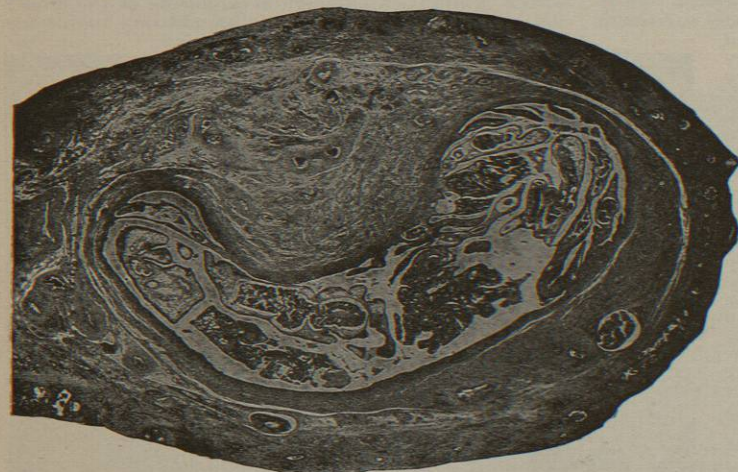


Fig. 1132.—Section of Ovarian Tube in a Case of Carcinoma of the Ovary. There are numerous tumor masses both in the wall and in the lumen. The involvement of the tube was most marked at the distal end. The process probably began in the lumen and from this extended into the wall. (80 mm. Leitz.)

tions where solid particles are carried by the force of gravity. There may also be extension by implantation along the surfaces covered by epithelium. In carcinoma of the kidney tumors may be found along the course of the ureters or in the bladder. In carcinoma of the ovary they may be found in the Fallopian tubes. The carcinoma often shows a marked tendency to extension along

the course of the nerves by means of the perineural lymphatics. The nerve as a whole may be surrounded and compressed by masses of epithelial cells or these may be found between the single nerve fibres. In carcinoma of the tongue involvement of the inferior maxillary branch of the fifth nerve is common. The extreme pain which so often accompanies carcinoma can be explained either by extension of the tumor into the nerves or by their compression in the contracting stroma. Tumor cells are rarely found free in the blood-vessels as they are in the lymphatics, but are usually associated with thrombi, and the main mass included in the thrombus may be degenerated. I have frequently found a vessel entirely occluded by a mass which was composed of fibrin and necrotic tumor cells, and along the wall of the vessel, where they could obtain nutrition from without, there could be seen a line of growing cells. In one case of carcinoma of the breast I found a small, round mass of epithelial cells, the centre of which was degenerated and filled with leucocytes, around this a small layer of fibrin, and on the outside evidently circulating blood. Such a mass was probably broken off from a fresh tumor thrombus and may have been actually in process of transportation.

It is important to determine, in carcinoma, whether the tumor originates in single cells or groups of cells which continue to grow, or whether it starts from a comparatively large area of tissue, or, finally, whether tissues of a similar character coming in contact with the growth can develop the same tendencies. It is very difficult to determine these points by microscopic examination. In carcinoma of the skin we undoubtedly often find large areas of epidermis in direct association with the tumor. It is also possible to find the epidermis in the vicinity of the tumor, but not immediately connected with it, apparently taking part in its growth, and growing in the same manner. The same thing is true in carcinoma of other epithelial surfaces, as in the alimentary canal. Here we often find the tumor in continuity with the glands over a large extent of the surface, the glands apparently growing into the tissue beneath and branching in this. Ribbert, who holds that the origin of the carcinoma is due to the separation of single epithelial cells and their inclusion in the connective tissue, believes that this connection of the tumor with the epithelial tissues is really secondary, and due to the extension of the tumor to the surface with the formation of a connection between the cells of the tumor and the epithelial surface. It is certainly true that when metastasis takes place the parenchymatous cells of the organ invaded take no part in the growth. Thus, in the secondary nodules in the liver, the liver cells are never converted into those of the tumor. When a glandular carcinoma comes in contact with epidermis, although this may actually be invaded by the single cells of the tumor and be in contact with tumor epithelium, there is no transformation. In a carcinoma of the breast the glandular tissue is usually atrophic. The tumor tends to extend along the ducts which may be surrounded by lymphatics filled with tumor cells, and yet the epithelium of the duct may show no change. In other cases the epithelium certainly appears to take part in the growth. There may be a simple proliferation of epithelium leading to the formation of projecting papillary masses within the duct, or in combination with this there may be an outward growth of the epithelium into the surrounding tissue. The cells change their character, becoming larger and taking on all the characteristics of the tumor cells. Undoubtedly,

for most of these conditions the explanation of secondary tumor extension given by Ribbert applies. In favorable sections, and especially in series of sections, the tumor evidently extends from the outside into the duct, and the tumor epithelium grows over or replaces the epithelium of the duct. It is often possible to distinguish definitely between the epithelium of the duct and the tumor cells in connection with it. In other cases this explanation will not suffice. The clearest evidence of a participation of the general epithelial structures of a part in the growth of the tumor was given in a case of carcinoma of the skin, in which there were undoubtedly proliferation and outward growth of the epithelium of several hair follicles which were in the immediate vicinity of the tumor, but in no way connected with it. I have seen a similar condition in the ducts and alveoli in carcinoma of the breast.

I have already spoken of the necrosis in the centres of the cell masses (Fig. 1125). In addition to this there may be more extensive necrosis involving either entire alveoli or masses of alveoli with stroma. Such necrosis is due to disturbances of circulation, usually by compression of arteries or veins, or both, by the growing tumor masses between which they run. In other cases it is due to the formation of thrombi. The necrotic tissue may remain, undergoing but little change, or it may be absorbed and its place taken by dense cicatricial stroma. The boundaries of the necrotic tissue are often extremely irregular, unchanged tumor tissue projecting irregularly into it. Hemorrhage may accompany the necrosis, but is not common. Where the necrotic tissue comes in contact with the surface bacteria may enter, producing gangrenous softening accompanied by suppuration. Ulceration is a common accompaniment of both the glandular and the surface varieties of carcinoma.

When the tumor extends to the surface the epithelium over this gradually disappears by atrophy, and the tumor appears as a raw uncovered mass resembling somewhat the base of an ordinary ulcer, although it is smoother and paler. There is always on the surface a thin line of necrosis due to the action of traumatic causes. In addition to this there is more extensive necrosis extending irregularly from the surface into the tumor tissue. The cells of the tumor at the surface are placed under more unfavorable conditions as regards their nutrition than are the cells in any other part of the tumor, for they receive their blood-supply from one side only, and constriction of the vessels is constantly going on. Necrosis due to this takes place and assists in the extension of the superficial traumatic necrosis. The necrosis is always assisted by the action of bacteria, and extensive gangrenous sloughs may be produced. There is continuous new formation of tissue pushing up from below, so that the ulceration is usually not deep and gives but little idea of the extent of the loss of substance. The destruction of tissue may be so extensive that in spite of rapid growth the resulting tumor may be insignificant in size. In carcinomata of the lip the surface of the tumor may appear as an ulcer somewhat depressed, or be covered by a scab formed principally of a mass of cast-off epithelial scales. When a glandular carcinoma extends to the surface it is not usually covered by a scab, because but little exudation can find its way from the tissue beneath to take part in its formation.

Ulceration plays a very important part in carcinomata of the intestinal canal, especially in those of the stomach, and the results of the process differ somewhat from the results of the process elsewhere. The necrotic tissue is destroyed by the action of the gastric juice, leading to the formation of a smooth, clean ulcer, and the tumor grows in elevated masses around the edge of this. The process of necrosis may be so active that the ulcer may resemble a simple ulcer and only by microscopical ex-



Fig. 1133.—Longitudinal Section of a Large Duct in Carcinoma of the Breast. The cylindrical epithelium of the duct is partly preserved but in places it is covered by a growth of the carcinoma cells which extend into the lumen from the walls. (No. 3 Leitz.)

amination of the edge can its character be determined. In other parts of the intestinal canal necrosis with resulting gangrene is more common, though we may have in the rectum carcinoma with ulceration, of the same character as that in the stomach. In the alimentary canal the contraction which so constantly accompanies the growth and which is due to the conversion of the stroma into cicatricial tissue, leads to constriction and occlusion of the lumen. The occlusion is assisted by the action of the elevated tumor masses around the ulcer.

**Constitutional Effects.**—The effect of a carcinoma on the individual remains to be considered. The most constant condition accompanying it consists in emaciation and the production of cachexia. The cachexia is probably due to a number of conditions. The malnutrition is due in the first place to the loss of sleep induced by pain. The absorption of the toxic products coming from the necrotic tissue may interfere with the nutrition and produce a condition of chronic toxæmia. To this must be added the absorption of toxic substances from bacterial action, and finally a general infection produced by bacteria which have invaded the tumor. The evidence of such conditions is seen not only in general degeneration of the organs but in such special degenerations as amyloid. Changes in the blood are unimportant. In the later stages there may be considerable diminution in the number of red corpuscles. The leucocytes may remain normal or show some increase, this particularly when ulceration is present.

**Etiology.**—The cause of carcinoma remains in absolute obscurity. A fair measure of our absolute ignorance of the subject may be found in the number of theories which have been advanced, each of which has its advocates and each of which is favored by certain conditions associated with the tumor. The first of these theories and the one which probably still has the most adherents is the traumatic theory which supposes the tumor to be due to the continuous action of an irritant which excites the cells to proliferation. Virchow has been the most prominent defender of this theory and many surgeons have supported it. Carcinoma of the lower lip, which is practically confined to

males, is used in support of the traumatic theory, being supposed to be due to smoking. The development of carcinoma in the site of old cicatrices, particularly those resulting from burns, is also used in favor of the traumatic origin. Probably the facts of the infrequency of carcinoma in those parts of the body most exposed to trauma and its frequency in those parts least exposed are the strongest arguments against the traumatic theory. No parts of the body are so exposed to traumata of various sorts as the hands and feet, and yet the tumor is exceedingly rare in the former and almost never occurs in the latter. No parts of the body are less exposed to trauma than the mammary gland and the uterus, and the tumor is very frequent in these situations. Even in the pessary days of gynecology, when the uterus was possibly the most abused organ in the body, carcinoma of this was not rendered more frequent. In the example given of the association of carcinoma of the lower lip and smoking, the infrequency of the tumor in the upper lip, in spite of the fact that this must be as much exposed to the traumatic or irritative action of the tobacco, is not explained. Carcinoma is not more frequent in those who by reason of occupation or conditions of life are more subject to traumata. Another example often cited to show the influence of trauma is the association between gall stones and carcinoma of the gall bladder. This tumor is about four times as common in women as in men, and lacing in association with gall stones is supposed to be a favoring cause. It is undoubtedly true that gall stones are constantly found associated with the tumor, but this may be due to the fact that their formation is favored by the production of necrotic tissue which may serve as a nidus in the formation of the concretion. It has also been urged that in cases of metastatic tumor formation in the gall-bladder calculi are not found, but here again the infrequency of ulceration and other conditions which would favor their formation must be considered.

It would not do to dismiss the influence of trauma in the production of the tumor as altogether incredible, but if it plays any part it must be a very minor one, or it may help in the action of other causes.

There is much that may be said in favor of the germinal theory of origin. This assumes that in the course of embryonic development remains of embryonic tissues may be included within the normal tissues, and from such embryonic remains, or from certain cells which have retained their embryonic capacity for growth, the tumor may develop. In favor of this theory it may be said that such remains of embryonic tissues do become included within normal tissues and from them tumors often develop. This theory, though not original with Cohnheim, was taken up by him and advocated with all the force and charm which characterize his work.

Ribbert has of late advanced a theory of formation which may be said to be a modification of the germinal theory. He supposes that not only such embryonic remains of tissue may be included in other tissues, but in

the course of pathological processes epithelial cells may be separated from their connection with one another and enclosed in the connective tissue. The stroma, for him, forms an integral part of the growth, and the tumor usually begins with cellular infiltration of the connective tissue. There is much that is opposed to this theory of Ribbert's. The cellular infiltration around the edge of a young carcinoma, though commonly present, may be entirely absent. I have regarded it as due to the reaction of the connective tissue to the presence of epithelial cells out of place and which act as foreign bodies. It is not at all an uncommon thing in the course of surgical operations to have both collections of epithelial cells and single cells included in the connective tissue, as in the suturing of wounds of the skin or intestine, and the same thing probably takes place in any operation on a glandular organ. The cells may remain in the tissues for a considerable time and may even show evidences of growth, but they are finally destroyed by the phagocytic action of cells derived from the tissue. Another point against the theory of Ribbert is his assumption that the small-cell infiltration is indicative of activity on the part of the connective tissue and the cells are derived from this. They are really chiefly lymphoid and plasma cells, and the condition may not betoken any activity whatever on the part of the connective tissue. Boll, in 1876, spoke of the importance of the stroma in the carcinoma. He says also that in the development of the tumor there is

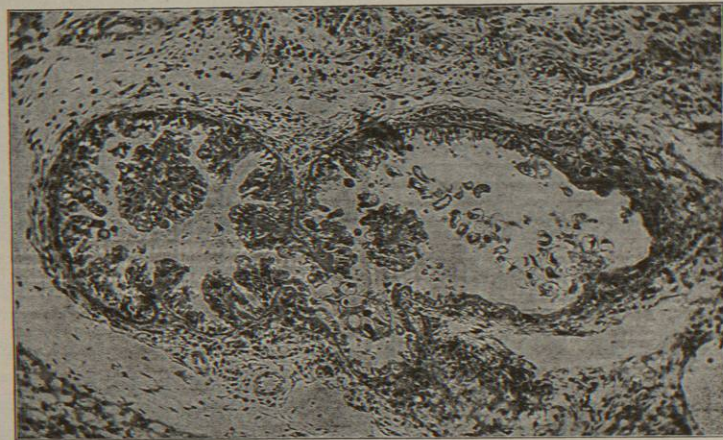


FIG. 1134.—Bile Duct of the Rabbit from a Case of Psorospermiosis of the Liver. The duct is dilated and partly filled with a papillary growth. The empty capsules are seen in the lumen. The younger forms are in the epithelial cells. (8 mm. Zeiss.)

marked proliferation of the connective tissue, leading to the formation of a vascular germinal tissue into which the epithelial growth takes place. He thinks that the formation of such a tissue is the one essential condition for the formation of carcinoma. When it is formed the old strife between the epithelium and the connective tissue breaks out anew. Thiersch, also, says that the frequency of carcinoma in old people may be due to degenerative conditions of the connective tissue which can no longer successfully oppose the growth of the epithelium. In this connection it must further be remembered that the epithelial cells of a carcinoma do not grow as does ordinary epithelium. The cells may retain something of their physiological tendencies as shown in their manner of growth, but they have a capacity for growth and an activity of growth far in excess of any normal tissue. Hansemann has called particular attention to the very marked difference in structure and in the manner of multiplication in the cells of the carcinoma as contrasted with normal epithelium. The enormous capacity for growth is not due to the abnormal situation in which the cells find themselves, but to certain qualities in the cells themselves. In their abnormal situation they are not placed in the most favorable conditions for nutrition, but in spite of this their growth is so rapid that the increase more than compensates for the cell destruction that takes place. Normal epithelium placed in the same situation shows only a limited power of proliferation and finally disappears.

This being the case, nothing was more natural than to suppose that some influence was exerted on the cells giving them other properties, and with this came the idea of the parasitic origin of carcinoma. In the first place, there seems much analogy between a carcinoma and such an infectious disease as tuberculosis. Both arise in some primary point, and from there the same process extends farther by means of the blood and lymphatic vessels. But the analogy does not go further. In tuberculosis the nodules are due to proliferation of the ordinary cells of the tissue and to exudation. The tissue formed has certain characteristics due to its arrangement and tendency to necrosis, but the same elements which compose it may be found in a variety of conditions. In carcinoma the new formation of tissue has a definite structure and could not arise from simple proliferation of the tissue elements. In infection of certain epithelial surfaces by protozoa there may be marked epithelial proliferation which may somewhat simulate a tumor, but the growth is typical and if the infection proceeds further the character of the formation in which it appears is modified by the character of the tissue. Examples of this are seen in the psorosperm infection of the alimentary canal and liver of the rabbit. In the infectious disease the pathogenic organism alone is necessary; in the carcinoma the cell is the infectious agent. The infectious disease may be transmitted from one individual to another. There is no evidence to show that carcinoma is ever transmitted from one individual to another under natural conditions, and even inoculation experiments which have been made from man to man and from man to animals have always been without any result. There have been cases, however, of successful inoculation from place to place on the same individual. In animals it has been possible to transfer carcinoma from one animal to another by implanting pieces of the tumor. Even if the carcinoma could be inoculated from man to man, or even from man to animal, it would be nothing in favor of its parasitic origin. When the disease once develops, when the epithelial cells once take on the peculiarities of growth which characterize the tumor, these cells are practically parasites. They live in strange situations and at the expense of the tissue which is their host, and have the power of unlimited increase. It might even be possible to suppose that favorable conditions for their increase might be provided outside of the body, and the disease might be transmitted by inoculation with generations of cells which have developed in vitro. It seems most remarkable that it is not possible to place these cells, still growing and contained in tissue, in another individual and have them retain their power. It is possible that there may be certain chemical differences in the tissue fluids of an individual with carcinoma which are favorable or essential for such a growth of the cells.

The carcinoma is easy of explanation after it has begun; the difficulty is in finding its primary cause. Ground for the assumption of a parasitic origin has been found in the supposed increase in the frequency of carcinoma. If it is due to embryonic causes or trauma or any such constantly acting cause, there should be no likelihood of increase. If due to parasites, carcinoma, like other infectious diseases, should show periods of increase and decline. There seems to be little doubt, from the numerous statistics which have been gathered on this subject, that there has been a marked increase in the mortality from carcinoma in the past twenty-five years. There are a number of things to be considered in connection with this increase. There has been an increase in longevity, due principally to diminished mortality in the infectious diseases. Carcinoma is essentially a disease of later life, and more people reach what may be termed the carcinoma age. The diagnosis of carcinoma, especially of the internal organs, has become more accurate and deaths are now properly attributed to this disease which were formerly put down under other heads. Deaths from carcinoma were formerly concealed as much as possible, due to a horror of the disease and fear of a supposed hereditary family taint being known. Hospital surgeons have

a general idea that the disease is increasing, from the increased number of cases which come to the hospitals for operation, due to the much greater success which now attends such operations. There still remains a great deal of work to be done on the statistical side, with a careful consideration of the operation of other causes, before we can say how much the disease is increasing or if it is increasing at all. The increase as generally shown is not in favor of the parasitic theory, for it has been gradually progressive, and not marked by exacerbations and remissions as would be the case with an infectious disease.

Although from a theoretical point of view all that we know about the carcinoma would oppose the parasitic theory, the proof of this is believed by some to have been shown by the actual presence of parasites in the cells themselves. No consideration need be given to the old works on this subject, in which bacteria were found in cultures made from tumors. No connection was ever shown between the tumor and the bacteria and no results followed from inoculation. Following this there have been numerous descriptions of other organisms than bacteria, and attempts have been made to cultivate these supposed organisms and to reproduce the disease by inoculation. At first these problematical organisms were supposed to be protozoa, and in some cases the entire life history of the organisms was described. Since the work of Busse the protozoic idea has been given up and most of the present writers on the subject describe the organisms as belonging to the blastomycetes. All of these descriptions depend upon certain bodies which are included in the cell protoplasm. These bodies included in the protoplasm differ in their size, form, and staining reactions. There are certain among them which have about the same size and apparently the same structure, and these have been especially selected as being varieties of the yeasts. They are not universally present in all carcinomata. They are found more frequently in carcinomata of the breast than in those developing from any other part, and have seemed to me to be more frequent in those tumors and portions of tumors in which degenerations are more frequent. They are not present in carcinomata of the skin. These bodies are in the vicinity of the nucleus and as a rule they have about the diameter of a red blood corpuscle, though they may be much smaller or larger. In some cases they are as large as the nucleus of the cell. They usually have a sharp edge separating them from the protoplasm and occasionally a small space may be seen at one side, but they do not lie in definite vacuoles. They have a homogeneous, non-granular structure, and usually there is a single granule in the centre of about the size of the nucleolus of a cell and which stains in the same manner. Not infrequently there are radiating lines which extend from the central granule to the periphery of the body.

Plimmer, an English investigator, has laid great stress on these bodies and regards them as the specific organism which produces the tumor. The number of these bodies varies enormously. In some tumors almost every alveolus contains several of them, in others they are wholly absent. They have no specific staining reactions. Plimmer has devised a special stain to demonstrate them, but they may be shown by the ordinary stain of hamatoxylin and eosin. They are certainly the most distinctive of all bodies included in the protoplasm, but there is nothing in their size, form, structure, or staining reactions which should lead us to consider them living parasites. The other objects included in the protoplasm may be divided into two classes. One class is composed of bodies generally round, sometimes single, sometimes in groups, always homogeneous and closely invested by the protoplasm. They stain in various ways, and many of them have a special affinity for certain dyes and in this way may be sharply differentiated from the protoplasm. Russel described certain of these which are sharply stained with fuchsin, and which have since been generally known as Russel fuchsin bodies, and he regarded them as probable parasites. Bodies similar to these may be found in a large number of pathological conditions,

and they are obviously nothing but various forms of degeneration of the protoplasm. The third group of bodies are the most variable of all. They always lie in vacuoles in the protoplasm. They are irregular in size, and careful study will show every variation between the most indefinite of these bodies and structures which may certainly be recognized as cells, and even the special variety of cells may be distinguished. The cells of carcinoma differ further from ordinary epithelial cells in their marked phagocytic properties. The included cells may be cells or portions of cells from the tumor itself, polynuclear leucocytes, or the lymphoid and plasma cells of the stroma. The last two groups of inclusions are easily explained; they are in no way peculiar to carcinomata or any of the tumors.

The various transformations which included cells may undergo can probably be better studied in the large cells of typhoid fever than elsewhere. They are also very numerous in the proliferating connective-tissue cells of granulation tissue. The bodies first described are more difficult of explanation and probably no single explanation of their origin can be given. I am convinced that many of them are due to degeneration of the nucleus. In a tumor which developed in a cicatrix after the operation, and in which they were very numerous, it was possible to see transitions in the nuclei leading to these bodies. The chromatin of the nucleus disappeared, the whole structure becoming homogeneous, and the nucleolus remaining as the central granule. They may also be referred to degeneration of segments of the nucleus which are occasionally thrown off and which represent the degenerative direct division. Borel believes that some of them are certainly to be referred to changes taking place around the centrosome, the radiate bodies being the spindle, and the granule in the middle the remains of the centrosome. In the giant cells of a sarcoma I have seen degenerations of the numerous centrosomes which become swollen up and the spindle around them more definite, but none of these bodies were found. Whatever the explanation given, there is nothing in the present state of our knowledge which should lead us to regard them as parasites. The defenders of the parasitic theory have been able, in a small number of cases, to cultivate yeasts from carcinomata. They have inoculated animals with these cultures and in a very few instances, not more often than could be explained as a coincidence, epithelial tumors have resulted. Almost invariably the new formation of tissue which has resulted from the inoculation has been granulation tissue of a sort which would follow from the introduction of any injurious agent.

It would not be justifiable to deny the possibility that carcinoma may be due to a parasite, but no evidence of this has been adduced up to the present time. On the contrary, everything we know of the tumor speaks against this idea. If a parasite is the cause, it must be different from any form of parasite we know, and its relations to the tissue must be different. It would be difficult to assume that a parasite could infect the tissues at a certain point, giving to the cells certain properties which would be retained by all following generations of cells. Otherwise we must assume a symbiosis between cell and parasite, as the parasite must be present in all cells and be carried with the cell to produce a metastasis, for a metastasis cannot be due to a parasite alone.

When the carcinoma once starts the cells themselves act as parasites. In the removal of a carcinoma, if the operation is to be successful, all the parasitic cells must be removed. It is not sufficient to remove the primary tumor and the lymph glands connected with the tissue, but the tissue between the two, in which the lymph vessels run and which may contain straggling cells, must also be removed. It may be extremely difficult to do this, for the blocking of the glands by metastases and the occlusion of the ordinary lymph channels may bring other collateral channels into play. The frequency with which the tumor reappears in the cicatrix after opera-

tion may possibly often be due to infection of the incised part by the knife of the surgeon.

W. T. Councilman.

CARCINOMA. (CLINICAL.) See *Cancer*. (Clinical.)

**CARCINOMA OF THE SKIN.**—A uniform nomenclature of malignant growths of epithelial tissue is, even in the present state of our pathological knowledge, by no means employed by writers.

In a general way, however, carcinoma is used to designate all varieties of malignant growths of epithelium, including both the glandular and the surface varieties. The majority of writers use the term epithelioma when referring to primary cutaneous cancers.

Fabre and Domergue\* make a clinical and pathological distinction between epitheliomata and carcinomata of the surface in the manner of growth (orientation) of the cells and the relationship of the cells to the basal layer of the epidermis.

In the present article carcinoma is employed as a comprehensive term embracing all the varieties which have their starting-point in the surface epidermis or its appendages.

**SYMPTOMATOLOGY.**—The primary forms which skin cancers assume depend to some extent on their seat and minute structure. We are unable, because of so many exceptions to this statement, to formulate any rule which will always associate a definite clinical type with a fixed histological structure.

The old division of carcinomata of the skin into (1) the superficial, flat, or discoid, (2) the deep-seated, nodular, or infiltrating, and (3) the papillary, is still largely employed as furnishing convenient terms for use in descriptions.

This classification is more or less imperfect, as the flat or discoid form may become deep-seated, the latter involving the skin secondarily as a superficial growth, while both are at times complicated by papillary outgrowths.

Unna† has attempted to reduce the majority of skin carcinomata to a few types according to the gross histological appearances or architecture of the growths. He obtains in this way three chief forms which he designates (1) the fungating, (2) the cylindrical, (3) the alveolar, each of which is further subdivided. A fourth or sub-form (carcinomatous lymphatic infarction secondarily affecting the skin after breast cancer and in metastases) is added to this classification.

The classification proposed by Unna is based chiefly on the histological structure of the growth, and in the fungating form the macroscopic appearance of the tumor is considered as well.

To one unfamiliar with the histological details of carcinoma of the skin the classification is too involved for practical purposes. A further reference will be made to it in describing the minute anatomy of these new growths.

To avoid confusion in the clinical picture of the malady certain primary types of more or less uniformity will be described, and then reference will be made to the forms which follow or develop on some pre-existing morbid condition of the skin or constitute the final stage of such affections, as xeroderma pigmentosum, Paget's disease, lupus vulgaris, syphilis, etc.

An important fact to be borne in mind is that carcinomata of the skin are not infrequently multifiform in their manifestation and often have a relatively benign course.

**Superficial Epithelioma.**—One of the most frequent forms in which carcinoma of the skin begins is as a small, hard, pearly gray nodule generally found on the upper two-thirds of the face in individuals over forty years of age. These nodules are often multiple, may remain for years with little or no change, or even may disappear spontaneously. If they are removed during their primary stage before ulceration begins they show only a slight tendency to recur.

\* "Les Cancers Epithéliaux," Paris, 1898.

† Unna, "Histopathology of the Diseases of the Skin," p. 670.

After a time one or more of these small growths may slowly increase in size, the centre at the same time sinking in and eventually becoming fissured or excoriated as the result of scratching or other irritation. At this stage, the new growth consists of a superficial ulcer covered with crusts made up of blood and secretions from the affected surface, and surrounded by a hard, elevated, waxy looking margin (Fig. 1, Colored plate XXI). The central ulceration may heal but is sure to recur, each time becoming somewhat larger, but seldom involving the deeper tissues; it has a red, granular base, secretes but little pus, and rarely causes pain. The floor and edges of the ulcer, consisting of soft friable tissue extending beneath the overlying epidermis, are easily removed by the curette. Instead of extending in a regular and progressive manner the ulceration may heal in the centre while continuing to spread at the margins, or one side may cicatrize, as a result of which gyrate and irregularly outlined ulcers with new foci may develop in the scar tissue (Fig. 1135). Such a carcinomatous ulcer may



FIG. 1135.—Superficial Epithelioma of the Face (Rodent Ulcer Type) of Fifteen Years' Duration. Showing scar tissue and peripheral ulceration.

generally be differentiated from syphilitic or lupus ulceration by the presence of the elevated, waxy, or pearly gray margin.

The progress of the affection is excessively slow, lasting ten, twenty, or even forty years before the patient dies from this or some other malady. It may eventually, however, invade the orbit, destroy the greater part of the skin of the face, the malar bones, the upper jaw, and penetrate the skull, causing the death of the patient from hemorrhage, exhaustion, or the involvement of vital organs. Fungating tumors reaching a considerable size may spring up from these ulcerating surfaces.

This variety of malignant growth, which has its primary seat near the eye, beginning as a minute, pearly gray nodule and spreading in a slow but progressive manner, is the so-called rodent or Jacob's ulcer, regarding the nature of which there has been so much discussion and divergence of opinion. It seldom or never invades the lymph nodes, and does not produce metastases or give rise to cachexia. It was looked upon by the older writers, such as Brodie and Paget, as a disease distinct from carcinoma and some modern authors even now deny its carcinomatous nature. Probably several varieties of superficial skin carcinoma during their course may assume the appearances described, so that the name, if retained, should be used in its clinical significance rather than to indicate a distinct species of epithelial new growth. Unna, on the other hand, opposes the view that every flat, superficial, carcinomatous ulcer should be called rodent ulcer. He believes that the latter affection has certain definite clinical

as well as histological features which are characteristic, and that it should not be confused with other varieties of carcinoma.

In addition to the early lesion in the form described, epitheliomata about the face may begin as brownish-red tubercles, hemispherical in outline, quite smooth, and of medium consistence. When first observed they are smaller than a split pea, slightly elevated, and may reach the diameter of half an inch before breaking down. These small nodules are readily scraped away with the dermal curette and apparently show little tendency to recur. They are seen about the ala of the nose, the eyelid, and the forehead. Sections of such growths under the microscope are found to contain proliferating bands, tubular processes, and acinous-shaped masses of small epithelial cells which correspond to those in the basal layer of the epidermis. These proliferating tracts and masses of cells are surrounded by a layer of columnar cells which represents the basal layer and probably limits their rapid growth. They are enclosed in a loose meshwork of connective tissue which is generally poorly developed or may be almost absent.

If undisturbed these nodules grow slowly for a number of years, then, under the stimulus of some irritant, increase more rapidly in size, finally resulting in open ulcers.

**Disseminated Epithelioma of the "Sebaceous Type."**—Multiple epitheliomata which are met with especially about the face, sometimes on the hands and trunk, are usually preceded by certain definite changes in the skin to which the name "senile keratosis" has been applied.

The skin at first becomes somewhat rough, and is covered by scales adherent to the follicular openings. Later, scabby concretions of a dirty yellowish-brown color form, and beneath them is found a warty condition which bleeds readily on slight irritation. Small cup-shaped depressions are subsequently noted beneath the thickened and altered horny layer; these coalesce and give rise to open epitheliomatous ulcers having hard, elevated edges and bases. A number of years may elapse from the time when the first changes in the skin appear before a malignant development takes place.

The same patient is frequently affected with several epitheliomatous ulcers in different stages of growth as well as with encrusted papillomatous areas which have not yet undergone the malignant change. The severer cases occur among those patients who are exposed to vicissitudes of weather and to the heat of the sun and in whom the earlier alterations in the skin which predispose to the condition are overlooked or neglected.

Other senile changes in the skin, as pigment deposits, papillomata, alterations in the blood-vessels, atrophy of the subcutaneous connective tissue, predispose to malignant new growths. These changes are allied to those which occur in the young in a more aggravated form, constituting the disease known as xeroderma pigmentosum, which, as a rule, terminates in the development of one or more malignant tumors. They are also met with in the condition known as sailors' skin, which Unna\* has observed and investigated. The changes which take place on the exposed portions of the face and hands are at first a cyanotic redness, followed by pigment deposits and leucodermatous spots. Localized thickening of the horny layer of the epidermis next occurs, and this, at certain spots, assumes a warty character, to be followed by papillary and ulcerating epitheliomata. While in their early stages these ulcers pursue an indolent course, and involve only the superficial tissues; at a later date they are more rapidly destructive than the rodent ulcers.

In Paget's disease of the nipple a superficial, moist, crusted, slightly scaling dermatitis may exist for a number of years as a precancerous condition. Healing cannot be brought about by the ordinary applications and eventually a superficial or deep-seated carcinoma appears in or beneath the chronic dermatitis. It is usually of the alveolar type, and more frequently begins in the lactiferous ducts than in the epidermis itself. Swell-

\* Unna, "Histopathology of Diseases of the Skin," p. 719.