

stead of thickened and covered by closely approximated granulations which enlarge until they assume a warty character. This papillomatous growth may spread laterally until almost the entire lip is covered with granulations before deep extension takes place. Instead of the ragged ulcer which is portrayed in Fig. 1137, a shallow,



FIG. 1136.—An Early Stage of Cancer of the Lip. Showing superficial ulceration.

oval and regularly outlined loss of tissue may constitute an early form of lip cancer (Fig. 1136). (Figs. 1136 and 1137 are reproduced here by the kind permission of the *New York Medical Journal*.)

Changes in the epidermis may be overlooked and the patient's attention may be first directed to a hard growth below the surface. This soon ulcerates, leaving a cavity surrounded by hard walls and base from which the degenerated epithelial cells forming the centre of the epithelial "pearls" may be squeezed out as comedo-like bodies.

In neglected cases the infiltration and ulceration involve the entire lower lip and the floor of the mouth; the teeth become loosened and all the adjacent tissues are destroyed. The submaxillary and submental lymph nodes are involved, as a rule, before such extensive tissue destruction occurs. The average duration of life in untreated cases is from three to five years, death taking place from sepsis or metastasis.

Cancer of the lower lip occurs in about fifty per cent. of surface epitheliomata. The male sex furnishes an overwhelming percentage of all cases, variously estimated at from eight to one to twenty to one. Statistics show that the large majority of those so afflicted are addicted to the use of tobacco, and of the few cases met with in women three-quarters were smokers.

**Diagnosis.**—The initial lesion of syphilis is often mistaken for cancer of the lip. Chancres of the lip are usually protuberant with an eroded or encrusted surface; they develop rapidly and very early involve the lymph nodes. The initial sore of syphilis is more likely to be met with in young adults, while epithelioma is a disease of later life. Numerous exceptions to these rules, however, are found.

Late ulcerating syphilides of the lip have also been mistaken for cancer, but these neoplasms of syphilis are usually multiple, rapidly break down or undergo absorption with atrophy, and lack the hard base which is always present in cancer.

In a doubtful case appeal should be made to the microscope.

**Prognosis.**—The course of carcinoma of the lip is much more rapidly fatal than is that of the flat variety of epi-

thelioma of the skin. An early and radical excision by the knife is the only method of treatment which promises subsequent immunity to the patient. If the operation is performed while the affection is superficial the outlook is not unfavorable. Even in such cases early operations sometimes fail to prevent general infection.

**PATHOLOGY AND MORBID ANATOMY.**—Carcinomata of the skin in the great majority of cases start from the surface epithelium or the epithelium lining the hair follicles. The sebaceous and sweat glands only exceptionally are primarily implicated.

It is not possible in all instances to associate a definite clinical type with a fixed histological structure.

Unna's plan of classification, which reduces the majority of skin cancers to a few types according to the architecture of the growths, involves the mutual relationship of the growing epithelium to the resisting connective tissue. A proper presentation of his views would involve an extended discussion, which is scarcely in place in this connection. A distinction of some clinical as well as pathological importance is that which separates these new growths of epithelium into two groups, in one of which the cells are chiefly of the squamous variety, while in the other they are of the small or columnar type. As a rule the squamous-celled epithelioma is found about the muco-cutaneous orifices, more readily involves the lymph nodes, and is more malignant than the small-celled variety of the disease. The difference in malignancy between these two types of growth is perhaps not so decided as it was at one time believed to be.

Squamous-celled epitheliomata are seen at a distance from the orifices. They may persist for a period of ten years without invading the lymph nodes, and then exceptionally the rodent-ulcer type of growth is met with in which the communicating lymph nodes are involved.

We are as yet ignorant of the factors which render rodent ulcer a relatively benign affection and the squamous-celled epithelioma a more malignant growth. The superficial seat of rodent ulcer and the early occurrence of ulceration are supposed by some writers to prevent the absorption of the cells by the lymph vessels. The resisting power of the connective tissue, which in rodent ulcer early assumes a structure like that met with in

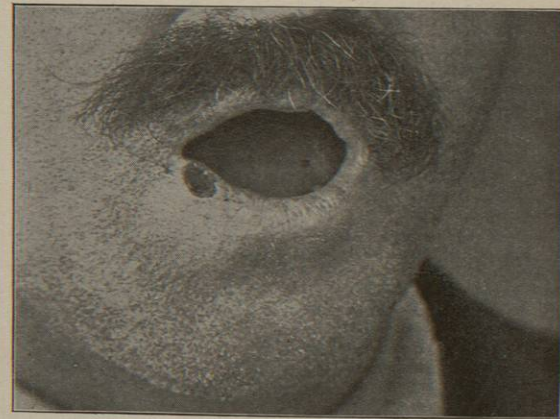


FIG. 1137.—Early Form of Cancer of the Lip. A shallow concave ulcer near angle of the mouth.

scirrhous cancer, is looked upon by Unna as an important factor in determining the clinical course of the affection.

Although the new growth of epithelium which we see in rodent ulcer is always made up of small cells which correspond to those in the basal layer of the epidermis or the outer root sheath of the hair follicle, it is possible that there are a number of other clinical varieties of small-

celled skin cancers which are not identical, at least clinically, with rodent ulcer.

Carcinomata of the surface epithelium, according to the classification of Fabre-Domergue, may develop in the direction of the adult type of cell, giving rise to cornification of individual cells or to rudimentary epidermic

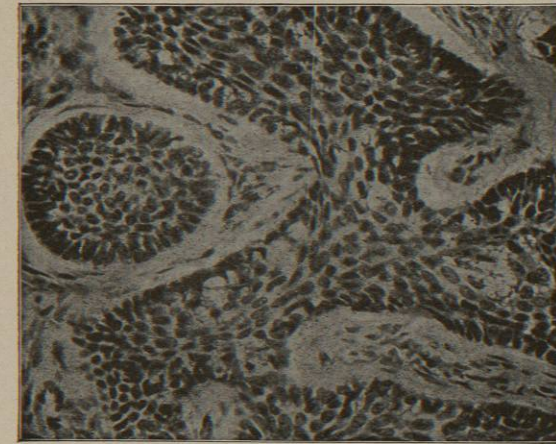


FIG. 1138.—From a Rodent Ulcer of the Face. Showing cylindrical processes of small epithelial cells surrounded by a basal layer. (Spencer one-quarter inch, projection ocular 2.)

"globes," between which type and the true epitheliomata there are many transitional forms. They may furthermore assume the embryonic type of growth and simulate so closely glandular carcinomata that it is not always possible to differentiate them by their histological structure.

In carcinomata of the adult there are, beside the embryonic type of cell, the same tendency to general cell activity throughout the growth, a non-continuity or absence of the basal layer, and consequently in both the same tendency to deep infiltration and general infection.

The clinical gravity of the tumor depends, therefore, on its structure rather than on its location.

The embryonic epithelioma (Fabre-Domergue), the tubular epithelioma of Cornil and Ranvier, and the small or columnar-celled epithelioma correspond in all essential points and are identical in structure with rodent ulcer in its earlier stages. The tumor originates from the lowermost layer of the rete Malpighii or from the outer root sheath and preserves with rare exceptions its embryonic cell structure throughout its entire course. The new growth of epithelium develops in the form of cylindrical processes throughout the lymph spaces of the derma (Fig. 1138). It is preceded by the appearance of a dense mass of mononucleated leucocytes (plasma cells, Unna). The connective tissue between the masses of growing epithelium becomes thickened and sclerotic and probably limits the down growth of the cylindrical processes, which may later assume elongated shapes owing to the greater resistance which they encounter.

The tubular processes of young epithelium are surrounded, in the earlier stages of the process, by a layer of cells which correspond to the basal cells of the epidermis (Fig. 1138). As the affection extends it is more difficult to identify this layer and it finally disappears. The loss of this protective layer is probably one reason for the more rapid extension of the growth in its later stages.

No good reason has as yet been advanced why the lymph nodes are not involved in rodent ulcer unless it is owing to the greater resistance interposed by the connective tissue. That they may exceptionally become infected was shown in a case which recently came under

the observation of the writer. A patient, sixty years old, presented a typical rodent ulcer, of ten years' duration, on the side of the nose, extending to the inner canthus. He had at the same time, behind the ear, an epithelioma with identical clinical features. The lymph node over the mastoid process was enlarged and after excision was found to be invaded by typical cylindrical processes of epithelium which could not be distinguished from those in the derma.

The exceptional situation of the epithelioma in this case, at a point where the integument is thin and where the growth was subjected to pressure against the underlying bone, was probably the factor which determined the invasion of the lymph node in the immediate proximity.

**Sweat-Gland Cancer.**—The case of sweat-gland cancer which came under the observation of the writer and to which reference has been made, had the following histological structure: Under a low power the derma was found to be the seat of numerous bands, masses, and gland-like arrangements of small epithelial cells which extended from beneath the epidermis to the subcutaneous connective tissue. They differed in their arrangement from that met with in other varieties of skin cancer, and suggested to the observer an attempted reproduction of glandular tissue. Under a higher amplification a complicated network was seen; it was formed by the interlacement of bands of epithelial tissue enclosing cavities which were partially or completely filled with degenerated cells or with a homogeneous substance allied to colloid matter. Cyst-like cavities were found in other parts of the microscopic field. They were lined by a single layer of columnar epithelial cells, and presented a striking resemblance to overgrown sweat ducts.

Fig. 1139 represents a group of enlarged and proliferating sweat ducts cut transversely. The columnar shape and regular arrangement of the peripherally located cells are well shown. These cells are situated upon a basement membrane, and are an almost exact reproduction of those normally met with in the sweat glands, although here very much hypertrophied. The lumen of the tubules is completely filled by the growing and multi-

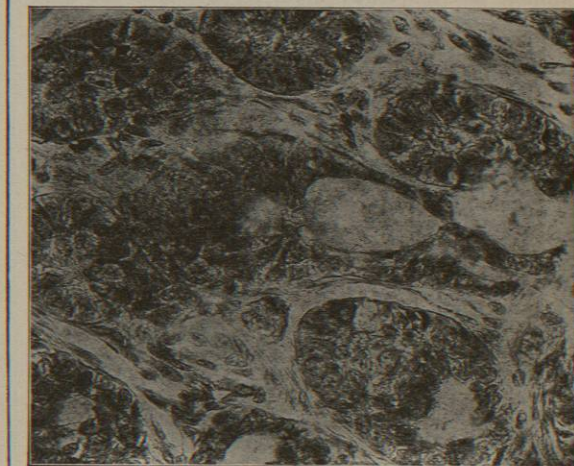


FIG. 1139.—From a Cancer of the Leg. Showing a group of enlarged and proliferating sweat ducts cut transversely. (Spencer one-quarter inch, projection ocular 4.)

plying cells, and in places the basement membrane is penetrated and the surrounding connective tissue infected by them. The other anatomical structures of the skin were not implicated in the cancerous process, neither was there any evidence of a tendency to cell-nesting or the formation of epidermic "globes." The epithelial processes met with in the small-celled carcinoma of the

skin, starting in the rete Malpighii, resemble to some extent the cell arrangements observed in the case under consideration. In the epidermic cancer, however, the cells are larger, and do not rest upon a distinct basement membrane, as in this case. Furthermore, the epithelial bands or tubules starting from the rete have no distinct calibre, and do not reproduce so perfectly the glandular structure.

**ETIOLOGY.**—The development of cancer of the skin is favored by a number of antecedent conditions to which reference has been made under Symptomatology. In a general way the statement is true that chronic irritation of slight intensity is one of the most potent factors which precede the malignant change in epithelial growths. The origin of highly malignant tumors from certain congenital moles has given some support to Cohnheim's theory of latent embryonic "remains." In xeroderma pigmentosum a congenital weakness of the skin is present which strongly predisposes to malignant growths. Heredity probably has some influence in favoring the evolution of some forms of malignant disease.

Inflammatory changes in the papillary region of the derma, by impairing the integrity of the basement membrane, favors the downward growth of epithelium. Atrophic changes in the connective tissue in advanced life exercise a similar influence.

The advocates of the parasitic origin of cancer consider the association of the malignant affection with pre-existing lesions as accidental. According to them the changes in syphilis and other chronic skin diseases merely furnish a favorable soil for the superadded infectious agent.

Cancer of the skin is more frequent after the age of forty, though no time of life is exempt. Kaposi has observed it a number of times between the ages of eight and eighteen. Rodent ulcer begins, as a rule, about the age of forty, but it may make little or no progress for several years.

**DIAGNOSIS.**—Superficial cancer of the skin is frequently mistaken for late syphilitic infiltration and ulceration or for lupus. These late nodular and ulcerative syphilitic lesions are usually more rapid in their evolution and involution, are frequently multiple, and lack the characteristic elevated and waxy border which distinguishes malignant ulceration. When syphilitic ulcers or those of lupus are complicated with epithelioma the diagnosis is more difficult. Lupus generally develops early in life, pursues a chronic course, and spreads on the margins of the patch by brownish-red nodules deeply embedded in the skin. These nodules or tubercles are as characteristic of lupus as the waxy margin is of superficial epithelioma.

Tuberculosis verrucosa cutis might be mistaken for papillary cancer of the fingers or hands. Induration about the base of a wart or cutaneous horn should excite suspicion of a malignant change.

In case of doubtful diagnosis resort should always be made to the microscope.

**PROGNOSIS.**—In superficial cancer of the skin the prognosis is more favorable than in any other form of the disease, as the progress is slow and the lymphatic system seldom implicated. If the growth is radically removed in its early stages there is little tendency to recur.

Cancers from moles are decidedly malignant, as they early involve the lymphatics and may soon be followed by a general metastasis. Papillary cancers are usually rapidly growing, and when they infiltrate the deeper parts, if not removed, lead to a fatal issue within from one to three years.

Rodent ulcer in its later stages almost invariably returns after removal, though preserving its local seat.

It is well to bear in mind that a superficial growth may become deep-seated and pursue a rapidly fatal course, as in the galloping or phagedenic epithelioma described by Besnier.

**TREATMENT.**—Early and complete extirpation with the knife is the only method of treatment that should be employed in cancer of the mucous membrane of the mouth, or of the lip.

On other parts of the body, as the neck, scrotum, etc.,

when the skin is freely movable and union by first intention can be secured, an excision offers the most rapid, painless, and satisfactory method of cure. If the operation is resorted to before the lymph nodes are invaded and if the incisions are made at a sufficient distance from the morbid growth, a cure may be looked for in the majority of cases.

Associated lymph nodes when invaded should be removed in as thorough a manner as possible.

Partial removal of cancer of the skin, even the most superficial, by the knife, curette, or caustics, accomplishes no good result and frequently stimulates these new growths to increased activity.

Superficial cancers of the skin are sometimes so situated that a cutting operation is followed by more deformity than after the employment of curettage and caustics. Many patients are so prejudiced against any cutting operation that they will endure the more prolonged and painful action of caustics rather than submit to the use of the knife. Under these circumstances the diseased tissue may be scraped away with the dermal curette and some suitable caustic applied to the resulting ulcer.

Numerous cures of cancer of the face have been obtained in this way by the writer, the caustics employed, as a rule, having been arsenic, in the form of Marsden's or Bougard's paste, or pure chloride of zinc. Arsenic is perhaps the best of all caustics as it is more certain in its action and presumably has a selective action on the morbid tissue. Marsden's paste is made by mixing two parts of arsenious acid with one part of powdered gum acacia and sufficient water to make the mixture of a firm consistence.

Robinson, who has devoted much time and consideration to the use of caustics in the treatment of cancer, prefers to vary the strength and duration of the application according to the cancer to be treated. He uses the paste in the strength recommended by Marsden and somewhat weaker, but never uses less than equal parts of arsenic and gum acacia. The paste is applied somewhat beyond the diseased area and is left on for from eight to twenty hours (Robinson). If the desired destruction of tissue is not obtained within the shorter limit a second but weaker application should at once be made until the necessary necrosis is accomplished.

The advantages claimed for the caustic treatment of cancer are the lesser degree of deformity which results and the greater certainty of reaching foci of diseased cells in the lymph vessels outside of the parent growth. It is, however, painful, and the separation of the resulting slough is somewhat slow.

Pain during the action of the caustic may be controlled by morphine, and the after-treatment should be conducted on the usual lines.

Before scraping away the morbid tissue as preliminary to the use of the caustic agent, the parts may be rendered anæsthetic by a spray of chloride of ethyl. If this is followed by the application of tampons saturated in a five or ten per cent. solution of cocaine the slight surgical procedure may be rendered absolutely painless.

Instead of employing destructive chemical caustics like arsenic and chloride of zinc the Paquelin or galvanocautery may be used to complete the treatment. The actual cautery is, however, not so certain to reach all the diseased cells as is the arsenical paste.

Patients who have been operated on for cancer should remain under observation for one or two years or longer, and the slightest recurrence should immediately be removed.

The internal use of arsenic for several months after the removal of malignant tumors has, perhaps, some influence in preventing or limiting recurrences.

John A. Fordeyce.

**CARDAMOM.—CARDAMOMUM.** The fruit of *Elettaria repens* (Sonnerat) Baillou (fam. *Zingiberaceæ*). Since the seed is the only active part, the above definition should be so restricted. The cardamom plant is a tall, reed-like, perennial herb, from six to twelve feet high. The flow-

ers and fruits are borne upon special short, scaly stems, partly prostrate among the bases of the leafy culms.

The plant is a native of Southern India, where also it has been long in cultivation. It has been introduced into other tropical countries. The cardamoms of commerce



Fig. 1140.—Malabar Cardamom. (Natural size.)

are mostly the product of cultivated plants, which are grown in the moist shade, either in clearings of the natural forests or in plantations of betel palms. The fruits are gathered before they are quite ripe. They are thoroughly washed, partly with soap and partly with a solution of a saponaceous fruit, and then bleached for some hours. They are frequently rubbed

between the hands with a mixture of starch and buttermilk. They are ovoid or oblong, pointed, rounded-triangular, three-valved, and three-celled capsules. The husk, when dried, is of a pale yellowish-gray or brown, flexible, and tough. Those which have been starched have a white and almost chalky surface. The seeds, five or six in each cell, are irregularly compressed, brown, and spicy. The fruits of the best varieties are usually short, about once and a half or twice as long as broad (1 to 1.5 cm. =  $\frac{1}{8}$  to  $\frac{1}{6}$  in.), very plump and full. They are commercially called "shorts." Others, longer and more angular, are denominated "short-longs" and "longs." The larger and longer cardamoms are mostly the produce of other species of *Elettaria*, and are therefore unofficial. Their odor and taste are not so pleasant. In selecting cardamoms, the point of chief importance is to see that they are short, plump, and well-filled, as otherwise the proportion of husk is too great, and the strength is thus weakened through the diminution of the active portion. This difficulty can be avoided by specifying the amount of the seeds instead of the fruits. The seeds from unfilled fruits are themselves defective, however.

Cardamoms are also distinguished, according to the countries or ports from which they are exported, as Malabar, Aleppo, Madras, etc. The former are the most esteemed.

The seeds contain about five per cent. of a pale yellow aromatic oil, of complex composition, which represents them in odor and taste. The ash of cardamom is rich in manganese. Cardamom is a typical aromatic, and is useful in all the conditions which call for articles of that class. As an agreeable flavor and appetizer, as a stimulant to digestion, and as a carminative in flatulence and in simple colic, it is sometimes, but not often, given alone. In combinations, as a pleasant and useful adjuvant and corrective, it is in more frequent use, acting favorably with cathartics, bitter tonics, stimulants, etc. But the principal use of cardamom is as a condiment or household flavor, for which purpose, especially on the continent of Europe and in the East, it is extensively employed. It is also used in flavoring liqueurs, and in curry-powder, etc. It is less irritating than the spices proper, and more so than anise and the milder carminatives. The dose of cardamom as an aromatic by itself would be from .5 to 1 gm. (gr. viij ad xv.). There is a ten-per-cent. official tincture which represents it completely. The compound tincture contains two per cent. each of cardamom and cinnamon, one of caraway, five of glycerin, and one-half per cent. of cochineal, in diluted alcohol, and is given in doses of 8 to 15 c.c. (2 to 4 fl. ʒ.). It also enters into the aromatic powder and the aromatic fluid extract.

W. P. Bolles.

**CARDAMOM, OIL OF.**—This term is understood as applying to the volatile oil, and not to the ten per cent. of fixed oil which the seeds yield. It is yielded to the extent of five or six per cent. It is of a pale yellow color, highly aromatic, has a specific gravity of about .900 and a rotation of +13°. Its important constituent is *terpinene* (C<sub>10</sub>H<sub>16</sub>). Its properties are identical with those of cardamom. It is, however, chiefly used for flavoring, especially liqueurs.

Henry H. Rusby.

**CARDIAC DEPRESSANTS AND CARDIAC STIMULANTS.**—I. **CARDIAC DEPRESSANTS.**—The term cardiac depressant is applied to drugs which lessen the force and frequency of the heart's action and are employed for this purpose in therapeutics. Since all classes of vertebrates and many invertebrates are provided with a nervous mechanism (the cardio-inhibitory apparatus) through which such changes in the heart are brought about in the normal animal, we should expect to find that those drugs which experience has shown to have the power of reducing the heart's action would exert their influence through this mechanism. As a matter of fact, the two drugs which are most used for their depressing influence upon the heart, aconite and veratrum viride, do exert their influence through the cardio-inhibitory nerves. It is conceivable that the part affected by these drugs might be any point in this mechanism—the nerve centres in the medulla, the nerve fibres, which in the higher animals are contained in the vagi trunks, or that which is rather vaguely (since the exact anatomical elements are not well known) termed the endings of the nerves in the heart. As is well known, nerve fibres are, as a rule, less easily affected by drugs than are nerve cells or the terminations of nerve fibres; and no drug is known which is able to exert a special influence upon the cardio-inhibitory nerve fibres, although there are many which stimulate the nerve cells in which these fibres originate and also their terminations in the heart. There are, moreover, drugs which seem to increase simply the sensitiveness of the vagus terminations without actually stimulating them, or at least without stimulating them sufficiently to slow the heart; the increased sensitiveness may, however, cause them to respond to a slighter stimulus than usual or with greater energy to a normal stimulus.

Another class of drugs, of which tartar emetic is a good example, depress the action of the cardiac muscle directly and so have been used as cardiac depressants; but such drugs are not considered as safe as those which work through, so to speak, more physiological channels. In fact, the depression brought about by a direct action upon the cardiac muscle is often associated with the condition known as collapse.

For the sake of completeness it may be added that the heart's action may be depressed by drugs acting in ways other than those just mentioned. Thus, if a drug causes a great fall of blood pressure the heart may be imperfectly supplied with blood and beat very feebly and slowly. If the blood pressure be much increased by a drug causing contraction of the arterioles, the high blood pressure may act as a stimulus to the vagus centre and so depress the action of the heart. The vagus centre may be stimulated reflexly by drugs having a powerful local action; it may also be stimulated by the accumulation of carbon dioxide in the blood if some drug which interferes with the respiration has been given. Again, it is probable that there are drugs which can slow the heart by depressing the accelerator nerves. Since these nerves are in a condition of tonic activity, any interference with their activity would lead to a slower rate.

While the most typical cardiac depressants exert their influence through the cardio-inhibitory mechanism, their action upon the organism is not by any means confined to this apparatus. Not only may many other functions—as, for instance, those of the central nervous system, the respiration, secretion, etc.—be influenced, but other parts of the vascular mechanism (the vaso-motor centres and nerves, the blood-vessels, the accelerator nerves of the heart, the cardiac muscle, etc.) may undergo changes which exert a profound influence on their action as cardiac depressants. In fact, a drug may stimulate the vagus and thus slow the heart and at the same time stimulate the cardiac muscle and in this way antagonize the effect of the vagus; sometimes one and sometimes the other effect will predominate. The condition becomes much more complicated when the preparation used contains several active principles, each with its peculiar action. For this reason it is desirable to use simple preparations and to determine as accurately as