ECTODERMAL TUMORS OF THE SKIN

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INTRODUCTION

The epidermis contains a basal-cell layer overlaid by squamous cells, and this in turn is covered with varying amounts of keratin. Beneath is the corium composed of connective tissue in which are embedded the skin appendages including the sebaceous glands, sweat glands and hair follicles. Neoplasms of the epidermis tend to form squamous cells and keratin and therefore are referred to as squamous-cell tumors or keratoses. They are usually found upon the surface of the skin. Tumors of the skin appendages, derived from the basal cells of the epidermis destined to form appendages often retain their basal-cell characteristics and are referred to as basal-cell tumors. They may be found on the surface or beneath the epidermis. Since the structures of both the epidermis (squamous cells and keratin) and the appendages within the corium are derived from the same basal-cell layers of the skin, it is convenient to divide neoplasms of the skin into epidermal tumors (squamous-cell lesions) and appendage tumors (basal-cell lesions). The term acanthoma is sometimes used for epidermal cancer and corium carcinoma or rodent ulcer for appendage cancer.

At the major orifices of the body (such as the mouth and anus) epidermal covering is modified to form the mucous membranes which are continuous with the modified entodermal coverings of similar structure. Epidermal and appendage tumors, therefore, may also occur in the mucosa of the eye, lips, oral and nasal cavities, pharynx, larynx, trachea, bronchi and esophagus, and on the mucous surfaces of the anus, vagina, penis, urethra, etc., although some of these structures are derived from the entoderm. Similar tumors may also occur on the mucous linings of the bladder, uterine cervix, ureter, and renal pelvis, although some of these mucous membranes are of mesodermal origin. Inclusions of epidermal tissue below the surface (both epidermoid cysts and remnants of the branchial clefts) may also provide a nidus for such growths. The basic histologic varieties of epidermal and appendage-cell tumors have, therefore, an exceedingly wide distribution in the human body. Malignant lesions of this type taken as a group constitute one of the most frequent forms of cancer in man.

Subvarieties of epidermal carcinoma in which keratin formation is absent are sometimes referred to as transitional, cuboidal, or mixed-cell

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cancer. While most common on the mucous surfaces, such structures also occur in rapidly growing and undifferentiated carcinomas of the epidermis (so-called Grades III and IV). Non-keratinizing epidermal cancer overlying lymphoid tissue, as in the tonsil, was named by Regaud of France, in 1921, lympho-epithelioma. In more slowly developing cancer the malignant squamous cells may be found entirely within the epidermis, a form of cancer described in the nipple by Paget (1876) in England, and in the skin by Bowen (1912), in America.

Subvarieties of appendage cancer include a form involving the nasal and oral mucous membranes and metastasizing to distant organs, adeno-cystic basal-cell cancer. When the relationship to sweat glands is marked the tumors may be described as syringo-epithelioma. Basal-cell tumors of the salivary glands contain a conspicuous amount of mucoid stroma and are usually referred to as mixed salivary tumors. Appendage tumors arising from remnants of the enamel organ about the teeth produce enamel-like substances and are referred to as adamantinomas. Aberrant mixed salivary tumors may occur, though rarely, in the skin distant from the salivary glands.

The microscopic variations may be classified as follows:

<table>
<thead>
<tr>
<th>Epidermal Cancer</th>
<th>Appendage Cancer</th>
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<tr>
<td>Keratinizing</td>
<td>Non-metastasizing</td>
</tr>
<tr>
<td>Acanthoma</td>
<td>Rodent ulcer</td>
</tr>
<tr>
<td>Paget’s or Bowen’s disease</td>
<td>Adamantinoma</td>
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<tr>
<td>Non-keratinizing</td>
<td>Metastasizing</td>
</tr>
<tr>
<td>Transitional-cell cancer</td>
<td>Adenocystic basal-cell cancer</td>
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<tr>
<td>Lympho-epithelioma</td>
<td>Aberrant salivary tumors</td>
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The present discussion is restricted to benign and malignant epidermal and appendage tumors of the body surfaces and is based upon a series of 2,100 cases recorded in the Surgical Pathological Laboratory of the Johns Hopkins Hospital. Approximately 1,000 of these lesions were located in the region of the head, including the surface of the scalp, forehead, face, ears, eyelids, nose, and chin. The remainder were equally divided between the surfaces of the upper and lower extremities and the skin of the body proper.

Benign and malignant appendage or basal-cell lesions were found in approximately 750 cases and benign and malignant epidermal or squamous-cell lesions in an equal number of instances. In 600 cases, epidermal cysts below the surface of the skin (usually associated with the pilosebaceous apparatus) were found, so that altogether the epidermal lesions were nearly twice as frequent as the basal type. The relative incidence of these histologic types was as follows:

- Benign appendage (basal) tumors: 220
- Malignant appendage (basal) tumors: 535
- Benign epidermal (squamous) tumors: 325
- Malignant epidermal (squamous) tumors: 425
- Epidermal cysts: 600
TABLE I: Basal and Squamous Tumors

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<thead>
<tr>
<th></th>
<th>Basal</th>
<th>Squamous</th>
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<tr>
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<td>Benign</td>
<td>Malignant</td>
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<td>Scalp</td>
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<td>Nose</td>
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<td>170</td>
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<td>Chin</td>
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<td><strong>UPPER EXTREMITY</strong></td>
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<td>Shoulder</td>
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<td>Fingers</td>
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<td><strong>LOWER EXTREMITY</strong></td>
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TABLE II: Epidermoid Cysts

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<tr>
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<td>Scalp</td>
<td>70</td>
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<td>Body and extremities</td>
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Basal-cell tumors are most frequent about the head, particularly on the face, eyelids, and nose. Epidermal or squamous-cell lesions are also common in the region of the face and about the ear. On the upper and lower extremities epidermal lesions predominate. On the surface of the body appendage-cell and epidermal tumors occur in about equal number. Of epidermal cysts, the majority occur about the neck, the next largest group in the scalp and upper part of the face, and a somewhat smaller number on the body and extremities. Tables I and II and Figs. 1 and 2 indicate the distribution of the various histologic types of skin tumors. Fig. 3 gives the comparative age incidence.
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EPIDERMAL TUMORS

Non-neoplastic Hypertrophies: Severe and acute injury to the skin usually results in ulceration, but changes in the epidermal layers leading to hyperplasia and thickening may be brought about by numerous forms of mild and chronic irritation. Mechanical irritation to the surfaces of the skin, with its strong natural protection, usually results in a thickening (mostly keratinization) which takes the form of the easily recognized callus or corn (clavus). The simple multiple warts (verruca vulgaris) which occur on the hands in young people are a more localized and distinctively papillomatous type of hypertrophy of similar histologic structure, resulting from infection with a filtrable virus. These lesions, like the callus, show a marked increase in keratin deposit, thickening and hypertrophy of the squamous-cell layers of the skin, which project in definite tufts (Fig. 4), and an intact and single layer of basal cells which delimit the hypertrophied layer sharply from the corium beneath. These two types of squamous-cell hypertrophy, the
corn and the common wart, show no tendency to undergo malignant change and may be regarded as non-neoplastic in nature.

The more serious forms of keratoses are frequent in elderly patients. They are familiar to dermatologists as senile and seborrheic keratoses (Eller and Ryan) and are known to pathologists respectively as squamous (or epidermal) and basal (or appendage) papillomas. The lesions are usually multiple, definitely circumscribed, rounded or oval, and occur after the age of forty. They are potentially malignant.

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**Fig. 2. Chart Showing the Distribution of Benign and Malignant Appendage or Basal-cell Tumors of the Skin (Cf. Fig. 1)**

**Benign Epidermal Tumors or Squamous-Cell Keratoses:** The senile or squamous-cell keratoses (acanthosis) are located chiefly on the temples or face, about the ears, or on the back of the hands (on exposed surfaces), and are often attributed to the effects of sunlight on an aging skin. They are sufficiently frequent among farmers to be considered by some as of occupational origin (Haagensen). They vary from a few millimeters to a few centimeters in diameter and in color range from yellow to gray-black. Their surfaces are crusted with adherent scales.
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and they are rough to the touch. When the crust is removed the lesion weeps, giving rise to a very shallow ulceration. The surrounding skin is usually parchment-like or of a pigmented senile character (Fig. 5).

Under the microscope this type of keratosis usually shows deposition of keratin, increase in the squamous-cell layers, and a down-growing of the epithelium into the corium. It is this down-growth of cells, with a tendency for the finger-like projections to be outlined by ill-defined and reduplicated rows of basal cells, which constitutes the proliferative

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Fig. 3. Chart Showing Comparative Age Incidence of the Chief Histologic Types of Skin Tumors

or precancerous phase of the epithelial hypertrophy (Fig. 6). When cancer occurs in these lesions, the basal cells lose their limiting membrane and islands of squamous cells bud off and appear in the cutis or subcutaneous tissue (Fig. 7). Such a malignant change is of the squamous-cell or epidermal type (Fig. 8).

Other precancerous dermatoses occur in workers in the petroleum and tar industries. In these workers small warts or horny overgrowths follow some initial inflammatory lesion, and the skin in the surrounding area becomes thickened, dry, and stiff. Scaling and ulceration soon take place with a tendency to crust over, with intermittent healing. In such areas, as in the scar after a frank burn by hot pitch or paraffin, squamous-cell cancer will develop. Heller collected 37 such cases of probable tar cancer. Sir Percival Pott, over a hundred years ago, first called attention to the rôle of coal-tar products in cancer of the scrotum in chimney sweeps.

Similar keratotic areas with warty overgrowths and ulceration, and secondary cancer formation, may occur in multiple dermatosis due to
chronic exposure to arsenic or its continued ingestion. Thickening of the skin, cracking, and hyperkeratoses, as well as frank ulcerations, act as precancerous lesions in roentgenologists and their technical assistants after prolonged or severe exposure to x-rays or radio-active substances (Figs. 9 A–C).

Recent studies indicate the probability of a common factor behind the cancerous changes in keratoses in farmers and in radiologists and similar occupational lesions in pitch and paraffin workers. Cook, Kennaway and their co-workers have demonstrated by experiments with benzpyrene that this chemical principle, or a group of similar compounds, forms the basis of the carcinogenic properties of the various coal-tar derivatives active in producing occupational cancer. This and similar synthetic compounds, when repeatedly applied to the skin of rats or mice, yield a high percentage of experimental epidermal cancer.

The observation that sterol (which is chemically related to benzpyrene, the active principle in coal-tar irritants) may be converted into ergosterol by irradiation with ultra-violet light, suggests that the cancer-producing powers of radiation are dependent upon the production in the tissues of sterol or cholesterol derivatives biochemically akin to some of these carcinogenic agents.

Other forms of dermatoses in which cancer may supervene and which have received special study are lupus, Bowen’s disease, and xeroderma pigmentosum.

*Lupus Carcinoma:* Both lupus vulgaris and lupus erythematosus are characterized by recurrent ulcerations with repeated healing and scar formation. Most authors estimate that approximately 2 to 5 per cent of such lesions undergo malignant change. So-called lupus carcinoma occurs in both treated and untreated cases, usually in lesions on exposed parts of the body, which have been present for a considerable length of time. There is a wide age distribution, both children and adults being affected. In some instances the course of the disease is
FIG. 5. **Squamous-cell Papillomas and Senile Keratoses Occurring in a Rural Practitioner**

These lesions occur chiefly on the forehead, cheeks, and neck (surfaces exposed to sunlight) in aged patients and are common among farmers. Every stage of lesion is present in this case. Path. No. 21989.

FIG. 6. **Area of Precancerous Change in Squamous-cell Keratosis, Showing the Proliferative Activity in the Basal-cell Layers**

There are large numbers of wandering cells beneath the epidermis. Path. No. 41274.
rapid and the prognosis is extremely grave. The histologic characteristics of the disease are those of benign keratoses with malignant change, superimposed upon an associated tuberculosis.

**Bowen’s Disease:** A separate form of keratosis with malignant change was described by Bowen in 1912. The first two cases reported occurred on the buttocks and on the lower leg, and were of twenty years’ and ten years’ duration respectively. The affected area of the skin in both cases was about four inches in diameter, crusted and composed of a confluence of small pale and red nodules. The characteristic histologic structure was hypertrophy of the epidermis which contained many large cells with hyperchromatic nuclei, frequent mitotic figures, and occasional intercellular keratinization. The picture was similar to that previously described by Paget for carcinoma of the nipple.
There has been much discussion in the literature since Bowen's original contributions in 1912 and 1915 on the histogenesis and exact classification of the epidermal changes in the disease which bears his name. The lesions have been described most frequently on the mucous surface of the nipple, vulva, lips, nose, and tonsil in elderly adults. They have been considered by some as identical with arsenic and x-ray dermatoses. The histologic feature of intercellular keratinization occurs, also, in other forms of squamous-cell cancer and in all probability the specific features claimed for Bowen's disease may be found in other forms of epidermal carcinoma in which the malignancy is of low grade (Grade I) and has not extended beyond the confines of the epidermis. Broders has suggested the term carcinoma in situ for these changes, and the present-day tendency is to regard the lesions as a slowly developing carcinoma occurring on the basis of a chronic dermatosis. The disease is in every way identical with Paget's cancer of the nipple (Fig. 10) in its early stages.

**Xeroderma Pigmentosum:** Xeroderma pigmentosum is a congenital familial disease characterized by pigmentation, roughening, dryness, ulceration, and ultimately tumors of the epidermis which undergo malignant change. The disease runs a protracted but fatal course. The initial lesions appear in the first few years of life as yellow or brown pigmented spots or a protracted erythema on the parts of the face and body exposed to sunlight. About the fifth year of life the skin shows dryness, scaling, and the formation of telangiectases interspersed with elevated areas, and atrophic patches of leucoderma. The eyes are affected by conjunctivitis with photophobia, corneal ulcers, and erosion of the lids with ectropion. Basal-cell and squamous-cell carcinoma and melanoma may supervene from the fifth to twentieth year of life, the patients rarely surviving beyond this period. Weakness, anemia, and inanition mark the terminal phases.

Under the microscope the squamous-cell and basal-cell layers of the skin are seen to be atrophic in many places, the elastic tissue in the corium is increased, and pigment is found in the basal-cell regions.
except at the points of greatest atrophy. Dilated veins are the most prominent vascular change. In the warty areas typical squamous-cell papillomas are found. Basal-cell cancers with pigmented areas are not uncommon. Either this form of malignancy or squamous-cell cancer may be found in the ulcerated areas.

The occurrence of xeroderma pigmentosum is recorded twice in our own series. In one instance, brothers were affected, and in the other six children (including brothers and sisters) in one family died of the disease. In one of these cases mixed basal-cell and squamous-cell cancer and malignant melanoma occurred in the same individual (Figs. 11 and 12).

Fig. 9A. Precancerous and Cancerous Lesions of the Skin in a Radiologist

Warty, scaly and atrophic areas predominate on the fingers. Path. No. 35399.

The pathogenesis and etiology of the disease have been discussed by Copeland and Martin, who have reviewed the literature and reported four cases. The exciting cause of the condition appears to be exposure of the skin, in susceptible patients, to actinic rays. The reasons for congenital predisposition to the disease, however, are obscure. Photodynamic substances, such as hematoporphyrin (a decomposition product of hemoglobin), have been suggested as playing a rôle. Skin lesions have been produced in animals injected with this substance and then exposed to ultra-violet light. Copeland and Martin, however, found the blood and urine negative for hematoporphyrin in two of their cases, and Darier injected animals with the blood of patients affected with the disease, with negative results. Treatment consists of protec-
tion from sunlight by indoor living and by dark clothing. Eradication of keratoses and neoplastic areas by excision or radium is recommended. X-ray therapy is contraindicated, as it may accentuate the disease. The care of the eyes is important.

Epidermal Cancer or Squamous-cell Carcinoma: Although many cases of epithelioma or epidermal carcinoma of the squamous-cell type are apparently not preceded by keratotic changes, a sufficient number of cases beginning in some form of dermatosis are on record to furnish fairly complete details on the earliest stages of malignancy. Since the work of Broders and MacCarty, the degree of differentiation in the proliferating malignant cells, as well as the persistence of benign structures in the tumor, is considered as indicating the degree of activity of the disease. The prognosis, the degree of radiosensitivity, and the therapeutic indications vary according to this histologic grading.

Grade I malignancy in epidermal tumors includes the earliest changes seen in keratoses or papillomas which are losing their benign characteristics and giving rise to secondary cancer (Fig. 13). Bowen's disease belongs to this group.

Usually it is in keratoses or benign warts that the highly differentiated and low-grade squamous-cell cancers begin. The more undifferentiated and highly malignant forms are prone to appear where no previous skin lesion has been observed by the patient and the first warning is a small ulceration. This is in keeping with the general rule for malignant conditions, that when carcinoma or sarcoma supervenes in a previously benign neoplasm the condition is usually less malignant than when the cancer arises de novo. Among the Grade I carcinomas, the majority give a history of papilloma, keratoses, or scar following a chronic ulcer or some form of dermatosis.

In early malignancy (Grade I cancer) the laminated layer of keratin
overlying the lesion may be thin or thick and bears no relation to the amount of epithelial hyperplasia. The keratin may accumulate between the crevices of the papillary overgrowth and by such an accumulation of débris the lesion may be given enough pigment to resemble clinically a pigmented mole. The hypertrophied portions of epidermis extend into the cutis in an irregular manner and at points removed from the surface keratinization takes place, giving rise to epithelial pearls.

![Fig. 10. Low-power and High-power Photomicrographs of Bowen's Disease or Carcinoma in Situ](image)

The high power illustration (below) shows the large epidermal cells with malignant nuclei first described by Paget in cancer of the female nipple. Path. No. 54054.

(Fig. 7). About such downgrowths many basophils, lymphocytes and eosinophils make their appearance.

The changes described thus far are not inconsistent with the diagnosis of a benign squamous-cell papilloma. The malignant change occurs at the base of the lesion with interruption and change in the basal-cell layer, the appearance of epithelial colonies deep in the cutis, and, most important, the proliferation of a new type of cell, the morphology of which can be definitely classed as malignant. This cell has a large vesicular nucleus, with one or two distinct nucleoli or nuclei showing definite mitotic figures. Such cancer cells may complete their
cycle of differentiation in an abortive manner, and while the large malignant nucleus persists, a rim of keratin may be thrown about the degenerating cytoplasm, a phenomenon often seen in Bowen's disease.

Clinically, cancer in these lesions is accompanied by ulceration, superimposed upon a papillomatous or verrucous base. As the cancer progresses, the ulcer widens rapidly, but the tendency to papilloma formation is still evident in the high, rolled-up edges. Fixation of the surrounding skin and secondary infection with mixed organisms are common.

*Grade II* squamous-cell carcinoma includes a transitional group of lesions between Grades I and III. According to Broders, in these lesions differentiated and undifferentiated cells are present in approximately equal numbers. Under the microscope the differentiated portions are seen to form islands in which degenerating squamous cells about a keratinized pearl are surrounded in turn by more malignant, undifferentiated cells. These undifferentiated cells show distinct nuclei and binucleated forms in transition between basal and squamous cells (Fig. 14).

*Grades III and IV* are conveniently discussed together. The lesions begin usually as a small ulcer or a fissure developing in an area of localized hypertrophy, although they may develop in a previous benign tumor. Metastasis to the regional lymph nodes occurs early, and permanent cures even by radical measures are few, 10 to 20 per cent compared with 35 to 40 per cent in Grades I and II.
Microscopically Grade III malignancy is dominated by a diffuse infiltration of malignant transitional cells (Fig. 15), such as are found in the stroma about the more differentiated islands in lesions of Grade II.

The malignant cells are disposed in sheets or in a so-called alveolar arrangement rather than as separate islands. In general the nucleus is more prominent than the cytoplasm and mitotic figures are frequent.

Many authors single out this type of cancer under the head of cuboidal-cell or transitional-cell carcinoma.
The predominating cell is cuboidal with a nucleus of fair size with a prominent nucleolus. Intermingled with these are cells with a compressed and elongated nucleus with malignant characteristics resembling the normal basal cell. Occasional cells of the squamous type are present, and here and there a very small pearly body.

In Grade IV malignancy the malignant spindle cells are intermingled
FIG. 15. Grade III Epidermal Carcinoma in which Malignant Cuboidal Cells and Transitional Epithelium Predominate. Path. No. 10271

FIG. 16. Grade IV Epidermal Carcinoma in which Malignant Basal Cells Showing a Transition to Cuboidal Cells Predominate

Note the numerous mitotic figures. Path. No. 38178.
with those of the cuboidal type without the presence of keratin or differentiated cells of the squamous type. Often Grade IV squamous-cell carcinoma closely resembles a basal-cell cancer upon cursory examination, but under high-power magnification there can always be found the malignant cuboidal cells which are so prominent in Grade III malignancy (Fig. 16).

Histogenesis of Squamous Neoplasms: In all forms of squamous-cell neoplasms, a definite histogenic cycle can be traced, showing a differentiation from the basal cell through the cuboidal and squamous cell to keratinization. In the squamous-cell keratosis of the benign type, squamous cells and keratin production predominate. In Grades I and II the cycle is completely visible, and the end products of squamous cells and keratin are always formed. In Grades III and IV cuboidal and malignant cells approaching the basal cell in type predominate and the more highly differentiated products are scarce or absent. The mother cell of the neoplastic change, the basal cell, is present in some form in all of these lesions and therefore may be held responsible for the proliferation.

Prognosis and Treatment of Epidermal Lesions: Epidermal tumors prone to malignant change are best treated in their benign stages. All forms of epidermal cancer tend to metastasize to the regional lymph nodes and particularly about the head and face may extend to structures which are difficult of access and in which the eradication of the tumor by any means is uncertain. With lesions of the scalp or about the ear, involvement of bone or cartilage may occur. Such lesions are unfavorable for irradiation and are best treated by surgery combined with thermal cauterization. While distant metastases are rare and
are usually of late occurrence in epidermal cancers, in Grades III and IV extension to the regional lymph nodes may take place while the initial lesions remain relatively small. Estimated on the basis of the present series of cases and other large series, such as those recently reported by Nielsen and by Halberstaedter and Simons, the probability of permanent cure (five-year period) in epidermal carcinoma averages approximately 35 per cent. Previous unsuccessful therapy and clinically demonstrable metastases to the regional lymph nodes reduce this figure to less than 5 per cent.

Fig. 18. Benign and Malignant Basal-Cell Lesions Occurring on the Skin of the Body

The small dark tumor in the inter scapular region proved benign, and the larger growth near the shoulder malignant, after excision and microscopic study. Clinically these dark basal-cell lesions are difficult to distinguish from melanomas and angiomas. Path. No. 20936.

In the early stages benign keratoses are best treated by cleansing with soap and water followed by alcohol, and kept moist and soft with petrolatum. If the lesion persists, it may be treated by x-ray therapy unless it is due to exposure to such radiation, in which case unfiltered radium or radon may be substituted. In lesions which have begun to weep or ulcerate, biopsy is indicated. If the lesion is small, the biopsy should include complete excision. Squamous-cell carcinoma of Grades I and II is relatively radioresistant but does not extend rapidly beyond the field of irradiation. In this stage of local confinement the lesions may be treated by excision or by the surface or interstitial application of filtered radium element or radon. In the irradiation of all forms
of malignant epidermal tumors the object is to give lethal, intense dosage over a minimal period of time. In Grades I and II, treatment of the regional lymph nodes in early cases may be omitted. If, however, there is any doubt, surgical excision of the nodes is indicated.

Squamous-cell cancer of Grades III and IV is radiosensitive but extends rapidly beyond the field of irradiation. In such cases radium and excision may be combined for the local lesion. The regional lymph nodes should be irradiated with x-rays or the radium pack, followed by surgical resection. Or after external irradiation of the affected region,

![Fig. 19. BENIGN BASAL-CELL PAPILLOMA](image)

The small basal cells surround large horny cysts and contain a scattering of melanin pigment. Histogenically the lesions are related to the hair follicles. Path. No. 19493.

the nodes may be exposed and radium or radon implanted in the affected node. Similar treatment should be employed wherever there is gross evidence of regional metastasis, regardless of the microscopic grading.

**APPENDAGE OR BASAL-CELL NEOPLASMS**

Two distinct varieties of appendage lesions occur in the skin, one which is intimately associated with the epidermis and is papillomatous in formation and the other which is subepidermal in location and usually overlaid by a thin atrophic layer of epidermis. Either form may remain benign or become the seat of malignant growth in the skin. The most common variety is epidermal—the seborrheic keratosis or appendage-cell papilloma which simulates in many ways the benign squamous-cell or epidermal papilloma.

**Appendage or Basal-Cell Keratosis:** The seborrheic or basal-cell keratoses occur in adults, usually between forty and fifty years of age, on the skin of the cheek, nose, eyelids, or trunk. They do not appear
on the back of the hands. They are seen, in general, in patients with an oily rather than a dry skin and more frequently in younger persons than the senile keratoses (Fig. 3). On the face it is difficult to differentiate these growths from the squamous-cell variety, and they may be confused clinically with pigmented moles (Figs. 17 and 18). Under the microscope, however, the appearance is characteristic (Fig. 19). The thickened epidermis contains a proliferation of small, pointed basal cells with prominent nuclei and scanty cytoplasm, perforated at numerous points by cysts of varying size known as horny cysts. The keratin is increased over the hypertrophied area, but on the under surface the basal-cell layer is everywhere intact, although irregular in outline. Melanin pigment is scattered about the cysts. When the appendage cells proliferate as independent, irregular, finger-like projec-

Figs. 20 A and B. Low-power and high-power photomicrographs of a benign subepidermal appendage-cell lesion probably arising in association with the sweat glands

The cell nests have a typical alveolar arrangement. Path. No. 31481.

tions into the corium, early malignant change is to be expected, and is always of basal-cell type. The occurrence of cysts lined by keratin and of melanin pigment in these neoplasms relates them to hair follicles. They have been aptly termed by Mallory, hair matrix tumors.

Subepidermal Basal-cell Nodules: While the most frequent benign basal-cell lesion is an epidermal, keratotic area, there are many nodules found just beneath the epidermis which have a similar microscopic appearance. These subepidermal nodules are composed of cell groups resembling those in the appendage-cell papilloma. An adenomatous or alveolar arrangement is prominent. While some are described as sweat gland adenomas and some show a relationship to the pilosebaceous apparatus (Figs. 20 A and B), more often no exact indication of the mode of origin is ascertainable under the microscope. These lesions are usually overlaid by a thin covering of atrophic epidermis, and are limited by connective-tissue boundaries.
Sweat-gland Adenomas: Lesions described as adenomas of the sweat glands are particularly numerous in the dermatological literature. Solid and cystic forms may be singled out as microscopically identified with the sweat gland structure. The cystic form shows dilated, coiled acini lined by a single layer of cuboidal or low columnar cells. The cell lining may be reduplicated in the wall to form papillary projections or may be flattened and atrophic. The cystic coils, becoming enlarged, fuse and give rise to multilocular cysts usually classed clinically as a variety of the epidermoid cyst (Figs. 21–23).

The solid form resembles the common variety of subepidermal basal-cell nodule. Islands of tightly packed basal cells with connective-tissue boundaries are clustered beneath the epidermis (Fig. 20). At intervals these solid basal-cell islands show coiled cystic spaces with a type of lining and structure which indicates a relationship to the structure of the sweat gland.

Sebaceous-gland Adenomas: With the usual appendage-cell nodule of the skin there is often an increase in the number of sebaceous glands surrounding the lesion. There is, however, a definite adenomatous proliferation of these glands in instances where there is no abnormality in the basal-cell layer. This type of lesion has been called by Nomland, senile sebaceous adenoma. It is a benign, multiple subepidermal lesion occurring most frequently in adults. Nomland has summarized its chief characteristics as follows. "The new growths appear in adult life, usually beyond the fourth decade. The elementary lesions are small, yellowish, slightly translucent, usually irregular, flat sometimes umbilicated papules which are scattered irregularly over the forehead and face. The microscopic sections reveal a new growth of the
sebaceous glands, taking origin from the region of the hair follicles.'" Histologically, hypertrophied sebaceous glands containing cells with small dense nuclei and abundant lacy cytoplasm are crowded together in the corium. The connective-tissue boundaries of the glands remain intact, but their ducts are often shortened and widened (Fig. 24). The condition is probably far more common than is recognized, for removal of tissue for microscopic study is rare since there are no subjective symptoms.

From a clinical standpoint these subepidermal nodules differ from
the seborrheic keratoses in their smooth covering and the absence of scaling. If there is any tendency for these growths to enlarge they should be excised with a margin of normal tissue.

**Fig. 24. Area of Hyperplasia of the Sebaceous Glands Showing Their Relation to Hair Follicles (Above); Typical Sebaceous Adenoma (Below). Path. No. 39239**

*Turban Tumors*: Multiple, slowly growing, benign basal-cell tumors on the scalp, varying in size from a pea to a cherry, white to pink in color, solid to cystic in consistency, and 50 to 500 in number, have been described in adults under the name of turban tumors, endothelioma capitis, or cylindroma of the scalp (Fig. 25 A). Ronchese found 31
well described and typical cases in the literature. The tumors make their appearance between the ages of fourteen and thirty years, reach their full development between fifty and seventy years, and usually affect more than one member in the same family, females more often than males. Unsightly appearance, occasional rupture with prompt healing, secretion, and rarely fungation are the major features. Malignant changes have not been recorded in typical cases. Under the microscope the lesions are seen to be composed of encapsulated sub-epidermal basal-cell masses, with a hyalinized connective-tissue stroma, and small cystic spaces enclosing amorphous material. The proliferating basal cells are apparently derived from the pilosebaceous apparatus, although some authors believe the sweat glands provide a more probable source. Repeated excision of the larger tumors at separate sittings is preferable to irradiation. The tumors respond slowly to radium implantation but not to roentgen irradiation.

**Aberrant Salivary Tumors:** Tumors of the salivary glands are either benign or malignant and occur in adults. The benign tumors are composed of small basal cells associated with a large amount of myxomatous stroma (benign mixed tumors), while the malignant variety contains numerous nests of basal cells with a tendency to form small acinar or cystic spaces (adenocystic basal-cell cancer). Both types of tumors have a tendency to recur after surgical excision. They are most commonly seen in the region of the parotid gland. Aberrant
ECTODERMAL TUMORS OF THE SKIN

Salivary tumors are relatively frequent in the region of the palate; they have also been described in the paranasal sinuses and in the mastoid region. Very rarely they occur subepidermally in the extremities, the cheeks, the scalp, or the region of the neck. Of twelve aberrant salivary tumors seen in the laboratory, five were in the region of the palate, one in the antrum, one in the region of the mastoid, two in the neck, one on the scalp, one on the flexor surface of the elbow, and another on the dorsum of the hand. The patients were elderly adults and the tumors had been present on an average of ten years. The subepidermal tumors on the arm and hand were both two or three centimeters in diameter and recurred after excision. Microscopic examination showed small compressed basal cells surrounding small cystic or acinar spaces (Fig. 25 B) filled with coagulated amorphous material, or strands of these cells compressed by a faintly staining hyalin or mucoid substance. The lesions associated with the skin are usually of the benign mixed type but may rarely give rise to adenocystic basal-cell cancer. The true nature of these benign growths is rarely recognized, and they are mistaken for malignant endotheliomas.

Appendage-cell Cancer or Rodent Ulcer: Appendage-cell or basal-cell cancer may supervene in seborrheic keratoses, in the subepidermal basal-cell nodule, or may arise de novo. Usually this form of tumor

![Image](image_url)

**Fig. 25 B. Aberrant Salivary Tumor Excised from the Dorsum of the Wrist of a Patient Aged Seventy-Seven**

The lesion had been excised twice sixty and fifty years previously. Path. No. 12376.
appears on the face, about the nose or eyes. The high, hard rolled edge characteristic of epidermal carcinoma is seen late in basal-cell cancer, but fixation of the surrounding skin occurs early (Fig. 26). These

Figs. 26 A and B. Photograph of Patient and Photomicrograph of Ulcerating Basal-Cell Cancer

This lesion eventually destroyed the cartilaginous portion of the nose, but was checked by repeated irradiation and thermal cauterization. Path. No. 41974.

tumors do not metastasize to the neighboring lymph nodes, but spread by extension, eroding the structures in their path. Two common forms of appendage cancer are met with under the microscope. One of these is an ulcerated area in which finger-like projections of basal cells in
scattered and elongated islands are invading the cutis and subcutaneous tissue. Apparently this is the type of malignancy which may arise as a primary ulcer or follow in the path of a basal-cell papilloma. The

other type of basal-cell cancer shows a relationship to the benign subepidermal nodule and is alveolar or adenomatous in arrangement, with malignant colonies budding off into the surrounding tissue.

Under the microscope the appendage cells in these malignant tumors are remarkably similar to the basal cells seen in sebaceous keratoses and in subepidermal nodules. The cells have very little cytoplasm, and the nuclei vary from spindle to oval in shape. They are slightly larger, however, than in the benign tumors, with many more hyperchromatic nuclei, undergoing mitotic division and anaplastic distortion.

The diagnosis of malignancy in these instances rests upon the ulceration, the infiltration of the surrounding connective tissue, and the enlarged, dense, and anaplastic nuclei found among the tumor cells.

**Adenocystic Basal-cell Cancer:** Adenocystic basal-cell cancer is similar histologically to the carcinomas described under aberrant salivary tumors. The lesions are composed of cords or acini of basal cells and histologically are practically indistinguishable from a variety of rodent ulcer described by Krompecher, under the term adenoides cysticum. Recently Spies has attempted to separate metastasizing adenocystic cancer from cystic rodent ulcer with a similar microscopic structure. The distinction cannot be made with safety except by location. The lesions of this variety occurring on the mucous membranes of the nose, palate, and in the region of the parotid are prone to metastasize, whereas in other characteristic locations, as on the face, metastasis is extremely rare, regardless of the variations in microscopic
structure (Figs. 27 A and B). In the cutaneous basal-cell lesions where metastasis occurs there will usually be found upon careful microscopic study definite transition to squamous-cell epithelium, a form of lesion sometimes referred to as mixed basal-squamous-cell carcinoma (Montgomery). In the rare instances where malignant lesions of the skin contain both appendage and epidermal types of tissue, it is important that the prognosis and treatment be based upon the epidermal features rather than upon the basal-cell characteristics (Fig. 12 A).

Treatment and Prognosis of Basal or Appendage-cell Tumors: The benign basal-cell lesions of seborrheic keratoses are readily eradicated with the x-rays. Irradiation of the low-voltage type may be employed (140 kilovolts at 4 milliamperes, unfiltered or filtered through 1 to 3 mm. aluminum at 30 cm. distance) or higher voltage with greater filtration may be used. Radium, filtered through the equivalent of 2 mm. brass, at 1 cm. distance, may be used. In the more persistent areas, biopsy is indicated.

With the non-metastasizing basal-cell cancer or rodent ulcer, superficial x-rays or the application of radium in the form of a plaque is highly successful, in many instances. These tumors are relatively resistant to irradiation when occurring in the depths (invading bone or in the parotid gland) and in such locations are extremely difficult to treat. Lesions recurrent after adequate irradiation are often better handled with thorough excision with the cautery than by a repetition of radiotherapy.

The metastasizing basal-cell carcinomas usually on the mucous membranes (so-called adenocystic basal-cell cancer) are radiosensitive to the same extent as other basal-cell lesions. Approximately 80 per cent of typical basal-cell cancers are permanently cured.

**Epidermal or Sebaceous Cysts**

Epidermoid cysts or simple dermoids, as they are often called, may occur anywhere in the body, but in general are more common about the head, face, and neck than elsewhere. In a series of over 500 cases we have found slightly less than 100 such tumors in the neck and only 70
FIG. 29. Typical Epidermoid Cyst Showing the Characteristic Lining and the Presence of Secondary Infection

The lesion is associated with the pilosebaceous apparatus. Path. No. 36794.

FIG. 30. Low-Grade Squamous-Cell Carcinoma Arising in the Wall of an Epidermoid Cyst. Path. No. 38010
over the head and scalp. These tumors are usually of congenital origin and arise from the inclusion of the ectoderm below the surface but also may develop as retention cysts from sebaceous glands with obstructed outlets. They form soft, elevated nodules, freely movable, over which the skin shows an increased number of dilated sebaceous ducts from which a white waxy substance exudes upon pressure (Fig. 28).

Upon excision these nodules are found to contain within a definite cyst wall a cheesy, atheromatous substance which is friable and without definite structure. Microscopically they have a squamous-cell lining which is arranged in stratified layers and surmounted by degenerated keratin. The waxy contents represent a mixture of this keratin produced by the squamous-cell lining and the secretion of the sebaceous glands, the ducts of which open into the cystic cavity. Many of these cysts connect with the skin through ducts of adjoining sebaceous glands, and because of such an opening on the surface are prone to secondary infection (Fig. 29). Microscopic examination of such infected cysts shows degeneration of the squamous-cell lining amorphous material, and granulation tissue in which are embedded giant cells of the foreign body type. In about 3 per cent of these dermoid cysts malignant change occurs, giving rise to squamous-cell carcinoma (Fig. 30). Very rarely such a cyst beneath the epidermis may be associated with sweat glands rather than with sebaceous glands and be lined by basal cells rather than squamous epithelium (Figs. 31 A and B). In such variants appendage-cell cancer or adenocystic basal-cell cancer may develop. The tumors are better treated by excision than by enucleation, and must be differentiated, when infected, from the ordinary carbuncle.
Pilonidal Sinus

This type of congenital lesion in the sacrococcygeal region is caused by the invagination of the normal ectoderm in the embryo (Fox). This invagination usually disappears before birth but may persist into adult life. With the onset of puberty, developmental changes and secretion enlarge the sinus, with cyst formation followed by infection. The tumor commonly contains fine, silky, light-colored hair and a gelatinous material which is altered by infection. The lining consists of several layers of squamous or transitional cells with numerous sebaceous glands and hair follicles (Fig. 32). The entire lining tissue is derived from the basal cells of the epidermis and, unlike dermoid cysts of the ovary, these tumors do not contain heterologous tissue such as nerve, bone, or cartilage. Clinically, these lesions are characterized by a discharge in the fold above the rectum from one or more openings in the region of the sacrococcygeal joint. Signs of inflammation, such as swelling or redness, may be present. A probe passed into the sinus may reach the bone. The direction of the probe is upward, which distinguishes the lesion from the downwardly directed fistula-in-ano. The best results in treatment are obtained by block.

FIG. 32. TYPICAL PILONIDAL SINUS

The embryonal hairs are surrounded by granulation tissue. Path. No. 55739.
dissection of this area guided by a preliminary injection of the sinus tract with a mixture of methylene blue and hydrogen peroxide to indicate its extent.

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