

SQUAMOUS CELL CARCINOMA

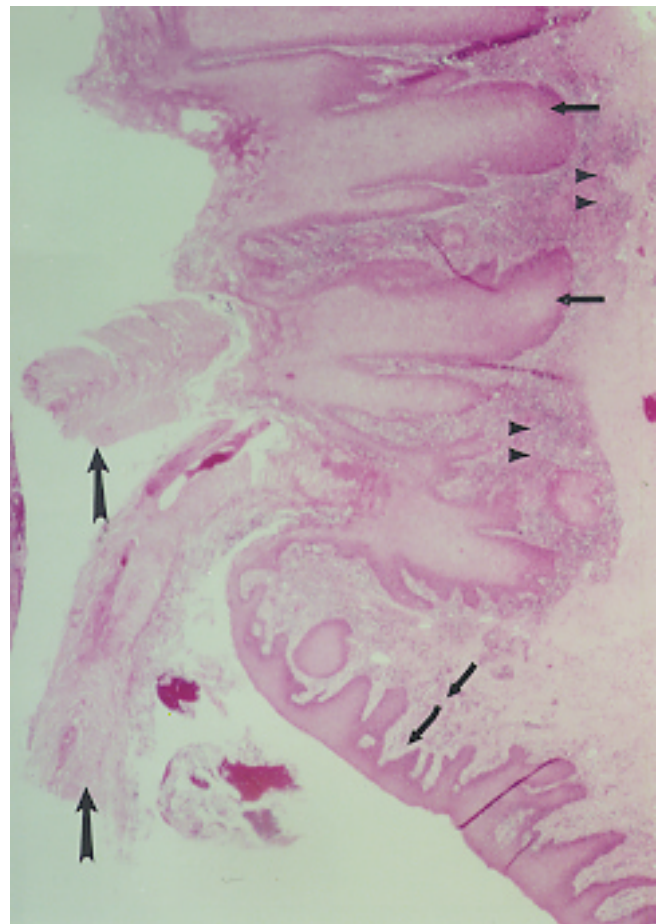
Squamous cell carcinoma may arise from dysplastic epithelium or independently of it. Except for basal cell carcinoma, it is by all odds the most common malignant condition involving head and neck tissues. Carcinogenics such as nicotine play an important part in the production of many squamous carcinomas, especially laryngeal and bronchial carcinoma, but other factors including heredity also are important. In mucous membranes of the head and neck, the disease affects men three times more often than women.

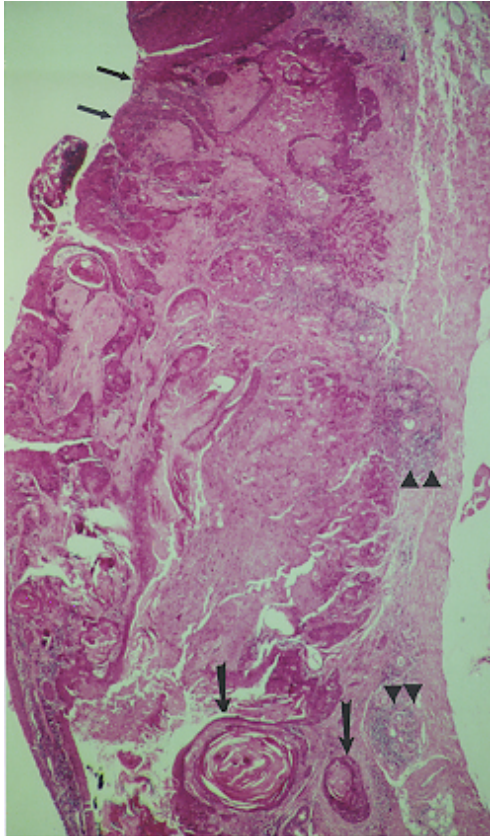
Squamous cell carcinoma spreads chiefly by direct invasion and by lymphatic permeation but also by blood vessel embolism. Metastases are most common to regional lymph nodes but also are seen frequently in the lung, and virtually any organ may be affected by metastasis.

Histologically, squamous cell carcinoma, if biopsied early, may be found to be no more than "superficially" invasive or "microinvasive," and sometimes is strictly limited to the epithelial surface and is called "insitu." More commonly, it is deeply invasive with islands, cords, sheets and formations of any description replacing normal tissue. Microinvasive carcinoma is a term used differently by different pathologists. Some would say that any breaching of the basement membrane by carcinoma qualifies the patient as having invasive carcinoma with no restriction on the depth of invasion, while others measure invasion in terms of 0.5 to 2.0 mm. and if it is no deeper than this, they may call it "microinvasive" or superficially invasive. Squamous carcinoma is "graded" according to the degree the squamous cells have departed histologically from their normal appearance. Normal skin and mucosa shows a reasonable thickness, a certain polarity or arrangement of cells one to another, intercellular "bridges," pale nuclei with a small nucleus in abundant pink cytoplasm with a nucleus-cytoplasm ratio strongly in favor of the cytoplasm, all cells and nuclei approximately the same size, with the shape of cells resembling fish scales or pavement blocks. Hyperchromatism, pleomorphism and increased mitotic activity (especially abnormal mitosis) favor malignancy. Keratin, the end product of squamous cell degeneration is characteristic of normal skin and some squamous mucosa (not the larynx), is also found in many carcinomas, especially the better differentiated lesions, i.e., those of lower "grade." Keratin is found scattered throughout many invasive carcinomas as eosinophilic, roundish, lamellated "pearls." A single squamous cell may contain its own tiny pearl of keratin. For some reason epithelial pearls are not customarily found in carcinoma in situ. Keratin pearls also are found in some instances of basal cell carcinoma where they might not be expected.

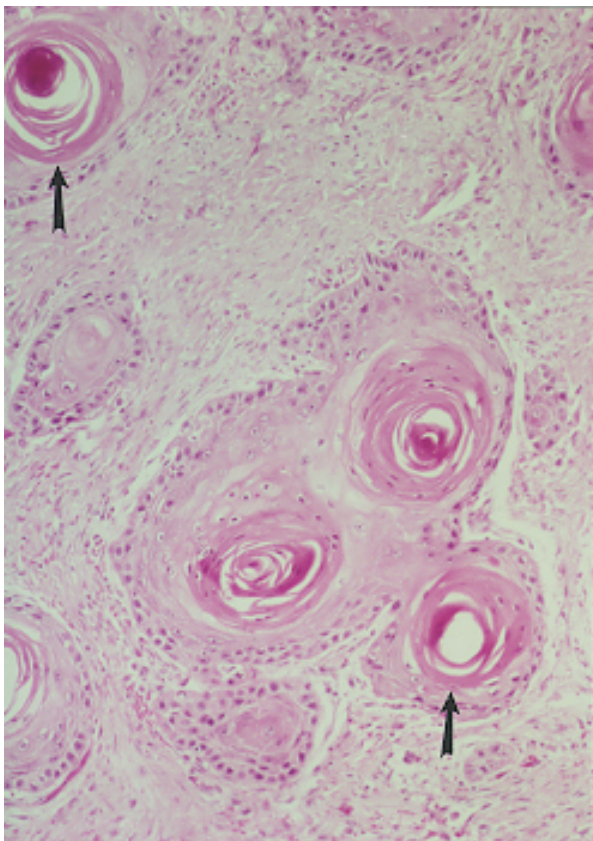
Characteristically, the nuclei of malignant squamous cells contains an abundance of DNA and are dark staining (hyperchromatic). The nucleus of a malignant cell is apt to be large in proportion to the cytoplasm so that the nuclear-cytoplasmic ratio may be 1:1 instead of 1:4 or 1:6, which is normal. In carcinoma the nuclear shape is apt to be variable and the chromatin coarsely clumped and distributed along the nuclear membrane. Also the nucleoli are apt to be as large, often with a pink color. Mitotic figures not only may be numerous, but they often are abnormal with large spindles in one area and shrunken spindles in others. Tumor giant cells may be present, some of which show a single huge polymorphic nucleus, and others with two or more nuclei. The orientation of the tumor cells one to another is erratic as compared to the orderly arrangement seen in normal tissue. Large masses or sheets of cells are seen and fingers or cords of tumor cells invade adjacent normal tissue. In favor of low grade carcinoma would be the finding of intercellular bridges, cells closely resembling those found in normal epithelium, and adherence to at least some degree of polarity. Higher grade lesions, III or IV on a scale of I to IV, show deviation from normal epithelium to the point that it may be difficult to determine if the origin is even from squamous epithelium. Then terms such as "high grade," "anaplastic," and "poorly differentiated" are used. The individual pathologist's experience and criteria of evaluation will account for occasional differences in grading of the same specimen among several pathologists.

Squamous cell carcinoma, verrucous, vocal cord. This carcinoma appears minimally invasive. Note the so-called "church spires" projecting externally from the surface of the tumor (large arrows) and the heavy inflammatory reaction (triangles) about the lower projections of the tumor. Because the tumor is so well differentiated, there is not the appearance of dysplasia such as would be expected in other squamous carcinomas. Rete pegs are rounded and wide giving the deeper margins of the tumor pushing" appearance (thin arrows). Compare with more normal epithelium just adjacent (double arrows) and note particularly the thinner, more "pointy" rete pegs.



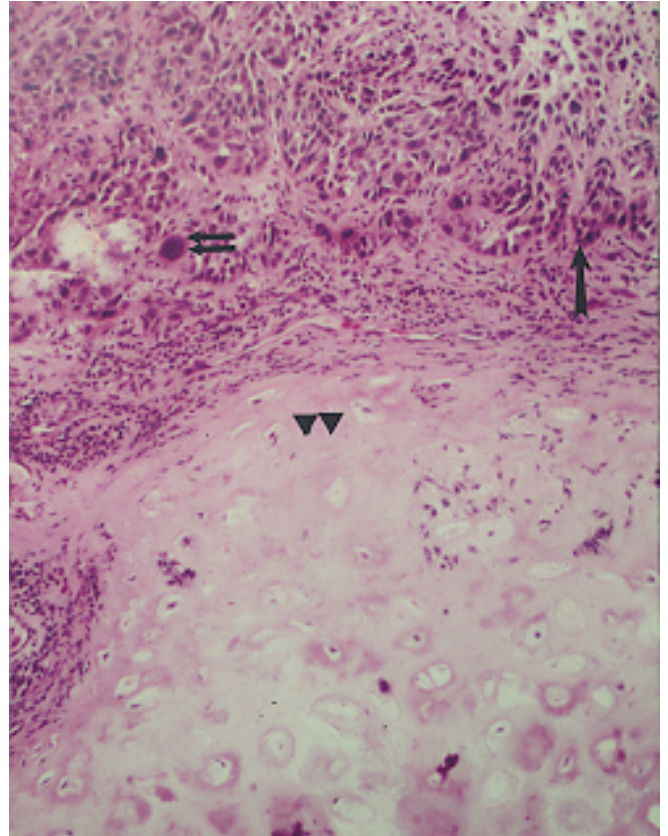


Squamous cell carcinoma, moderately differentiated, vocal cord. The invasion is more marked than at upper left. There is ulceration (small arrows) and keratin pearls are seen (large arrows). Inflammation is present (triangles).

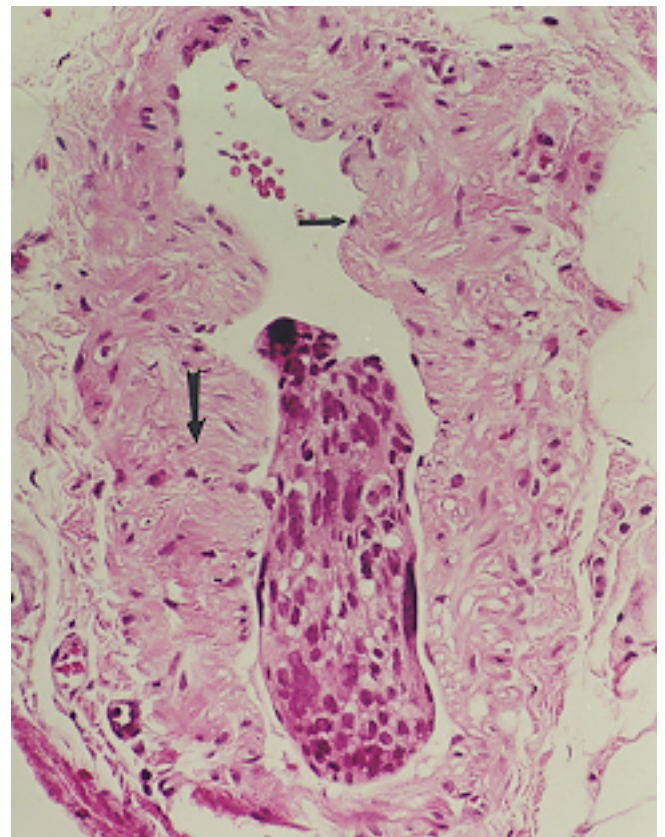


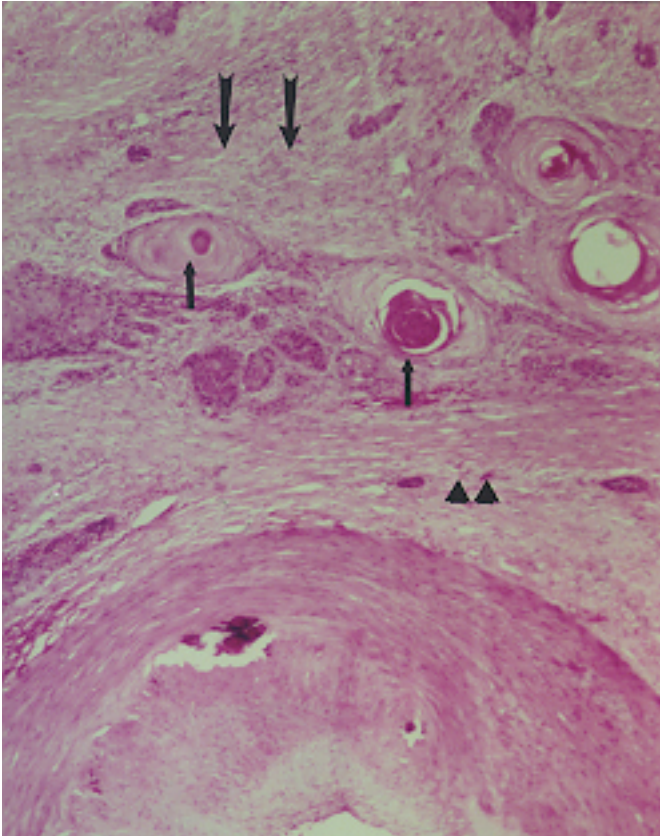
Squamous cell carcinoma, keratinizing, auricle. In spite of formation of abundant keratin pearls (arrows), this lesion showed peri vascular and perineural invasion and was graded as only moderately differentiated overall.

Squamous cell carcinoma, larynx, nonkeratinizing and graded as poorly differentiated. This area demonstrates invasion of cartilage (triangles). Note the hyperchromatic nuclei (large arrow) and pleomorphism (small arrows) and the lack of any regular arrangement of the cancer cells. Some have thought that cartilage or perichondrium may offer some relative resistance to invasion by malignant cells as compared to other tissues.

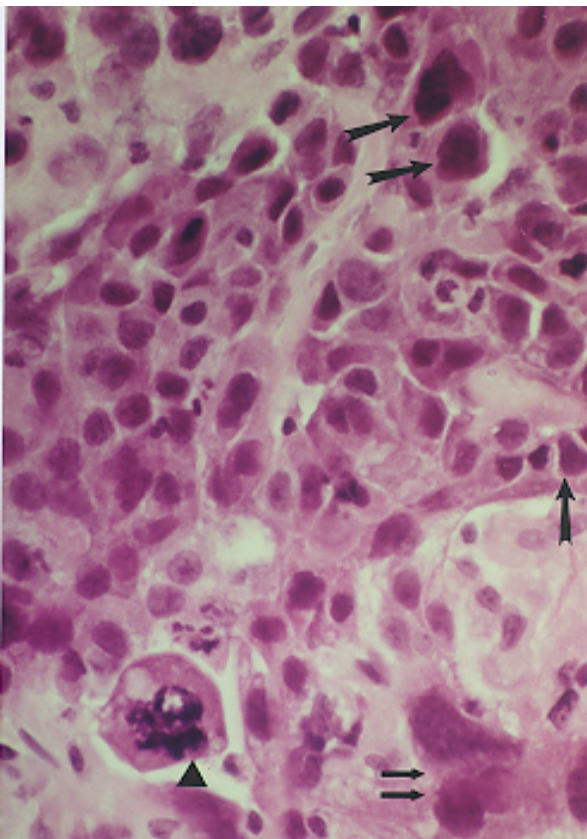


Squamous cell carcinoma, embolic in blood vessel. Hyperchromatic and pleomorphic nuclei are seen. The vessel is identified by its endothelial cells (small arrow) and well-developed muscular wall (large arrow). Also a few erythrocytes are present in the vessel further identifying this as a vein rather than a lymphatic channel.



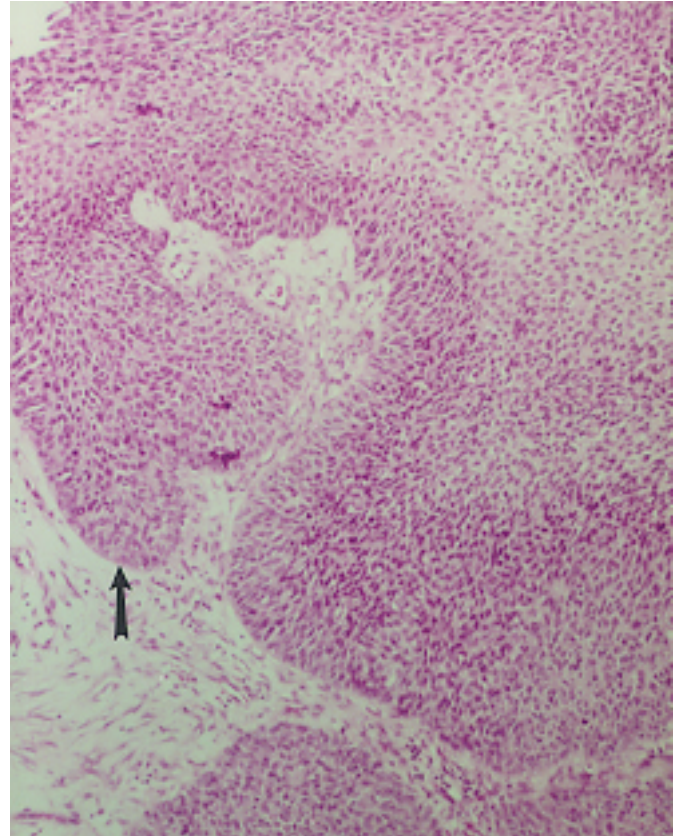


Squamous cell carcinoma, keratinizing, graded moderately differentiated, invading adventitia (triangles) of a large blood vessel. Marked desmoplasia is present (large arrows) and epithelioid pearls are seen (small arrows).

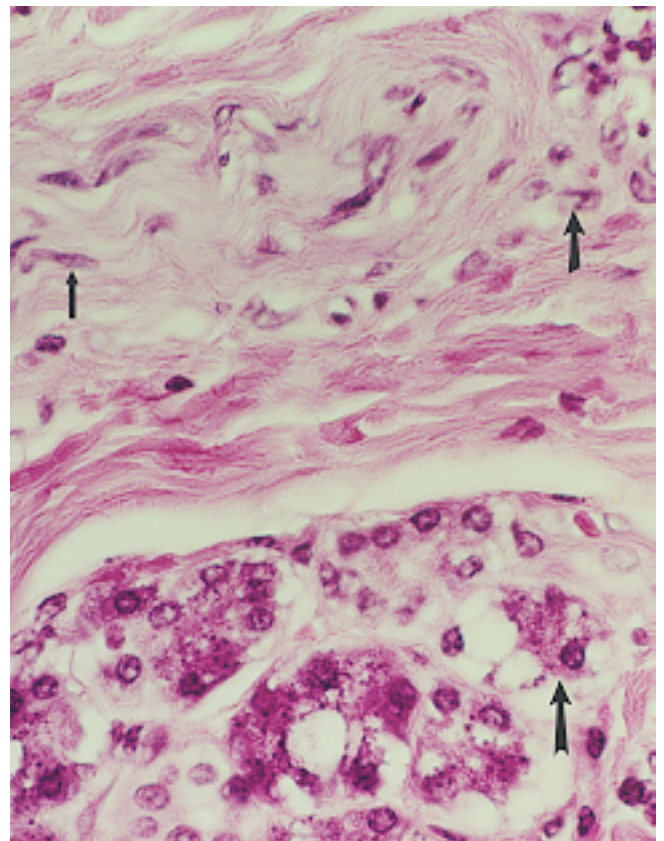


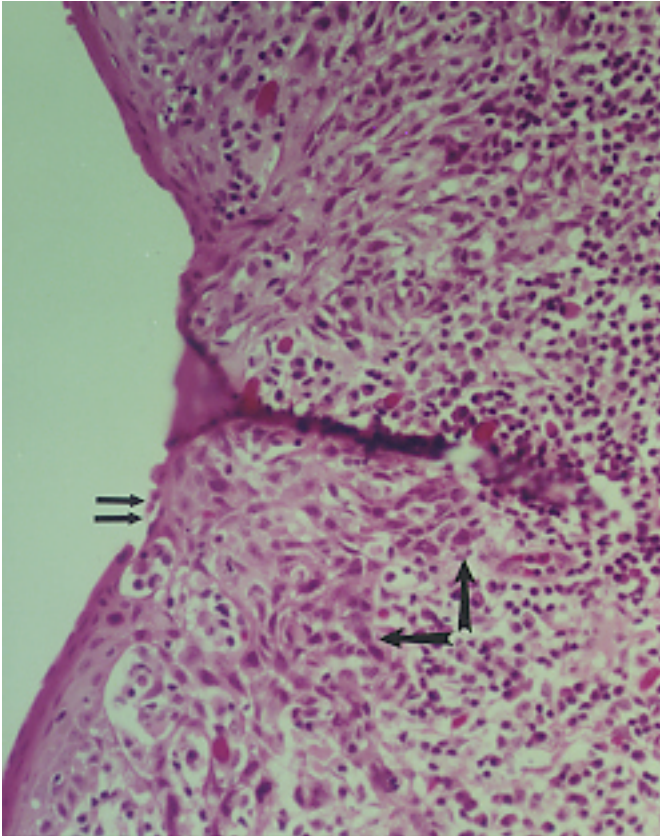
Squamous cell carcinoma, larynx, poorly differentiated. Note the abnormal mitosis (triangle), greatly altered nuclear—cytoplasmic ratio in which nuclei are often almost as large as the entire cell (large arrows), pleomorphism that involves virtually every cell, hyperchromicity of all nuclei, and complete lack of polarity. A multinucleated tumor giant cell is present (double small arrows).

Carcinoma in situ, sphenoid. The basement membrane remains intact (arrow) even though the carcinoma shows the same cellular alterations and lack of polarity as seen in invasive carcinoma. Full thickness of epithelium is involved.

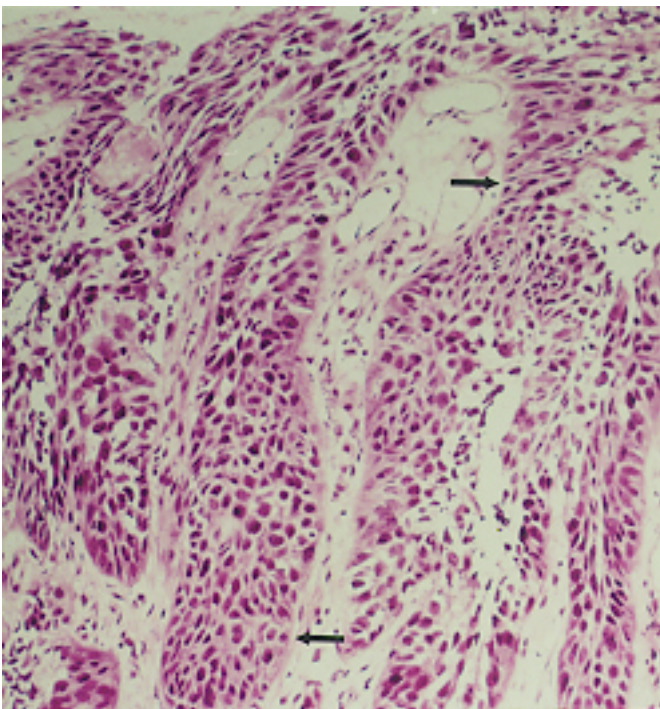


Poorly differentiated squamous carcinoma, invading nerve (small arrows). Here the cancer cells (large arrows) show no differentiation at all and may even be difficult to identify as squamous cells.



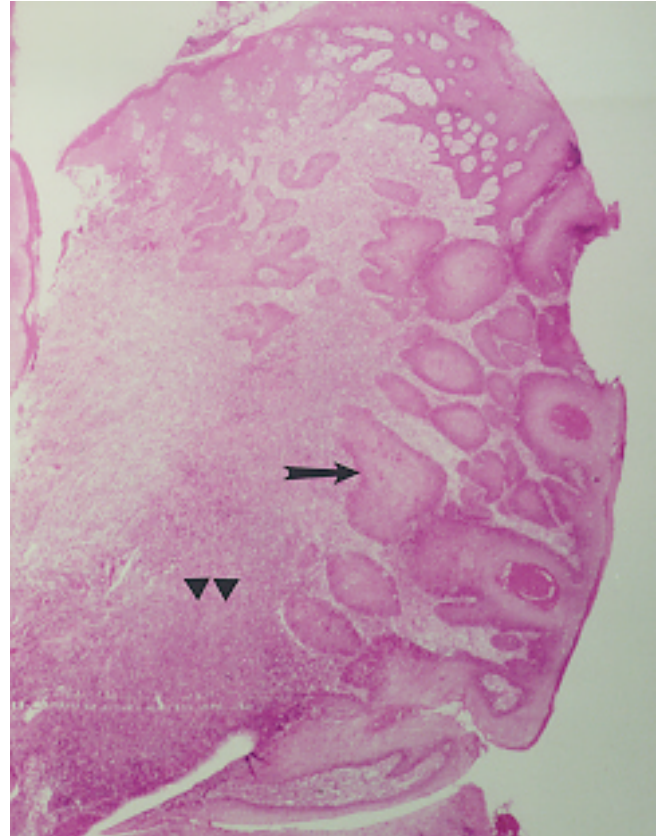


Squamous cell carcinoma, esophagus, early invasion (large arrows) with ulceration (small double arrows). Marked chronic inflammatory response. Squamous carcinoma accounts for well over half of esophageal carcinomas. Grossly, they are infiltrative, ulcerative, or polypoid and vary from well to poorly-differentiated. Metastases occur in nodal areas corresponding to the area of esophagus involved—lower third spreading to retroperitoneal and abdominal nodes, upper third to cervical nodes and middle third to paratracheal nodes.

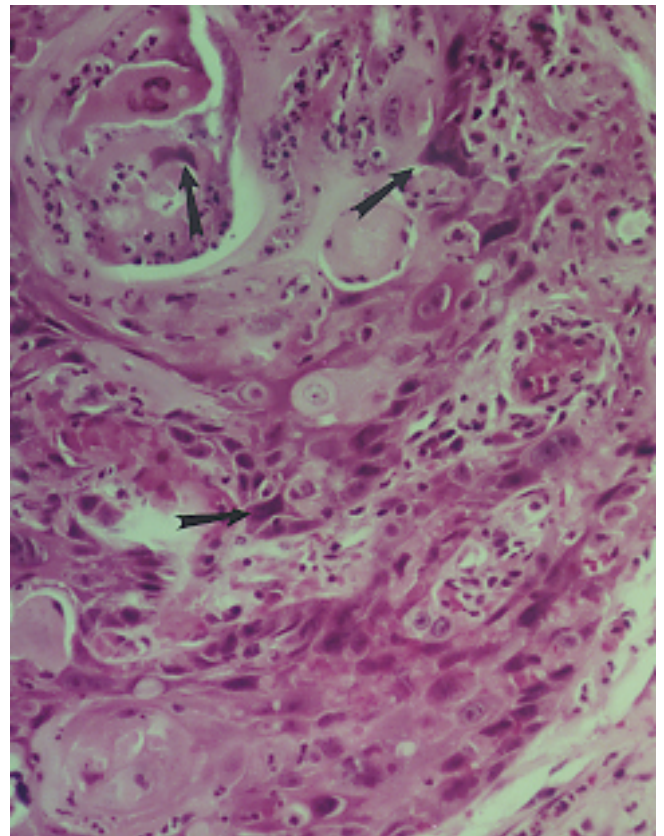


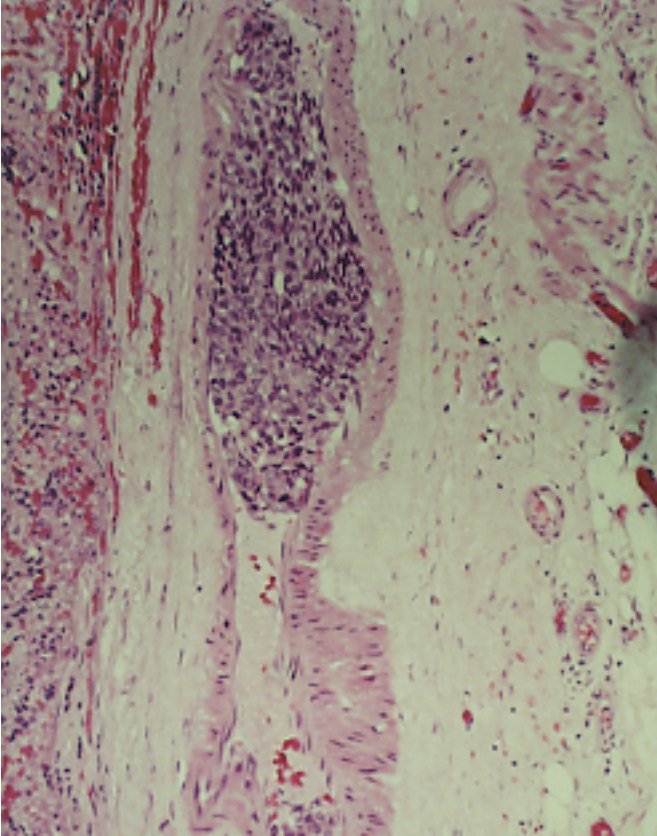
Carcinoma in situ, or severe dysplasia, larynx. The basement membrane remains intact (arrows), but there is severe disorientation of cells, hyperchromicity, and "top to bottom" involvement of epithelium.

Squamous cell carcinoma, superficially invasive. Authorities differ somewhat as to what depth of invasion ought to be considered as superficial. There is characteristic inflammatory reaction (triangles) surrounding the invading nests of tumor cells (arrow).

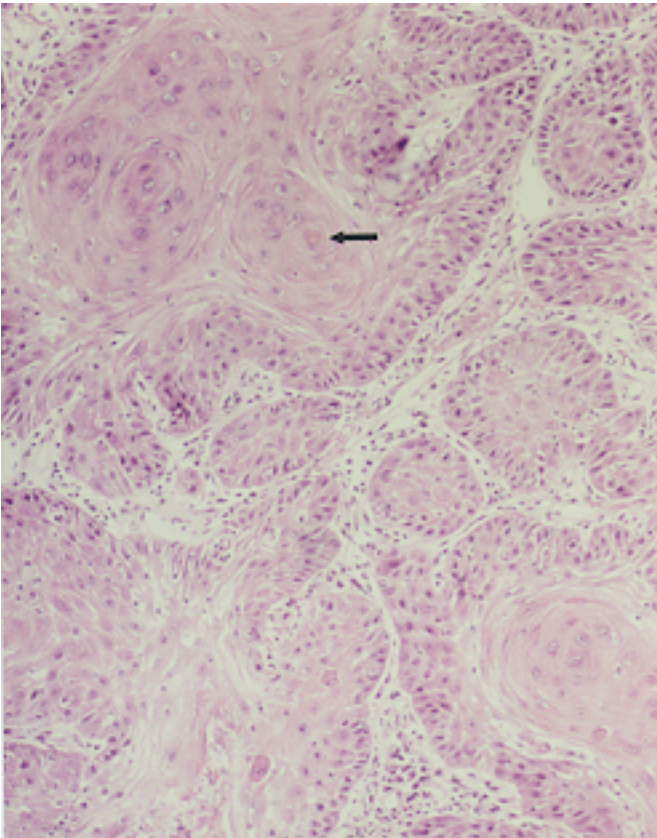


Squamous cell carcinoma, larynx, with a “wild” appearance because of marked cellular pleomorphism and hyperchromatism (arrows); intercellular bridges and pearls are also visible.



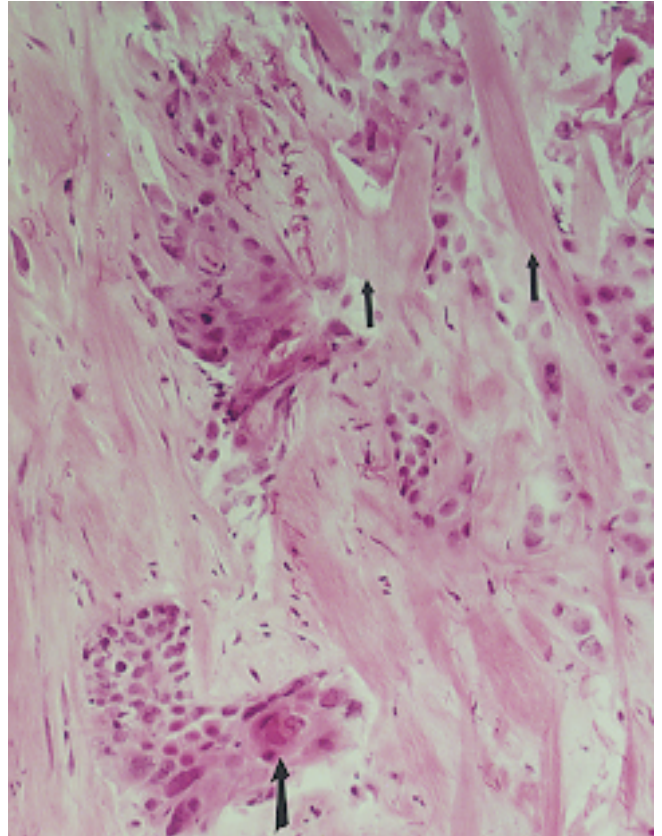


Squamous cell carcinoma, filling blood vessel.

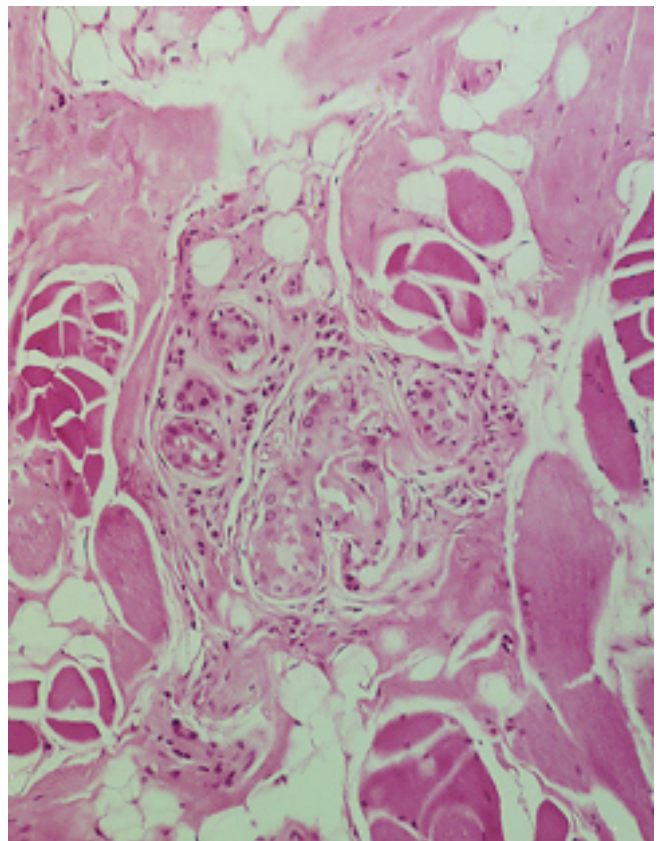


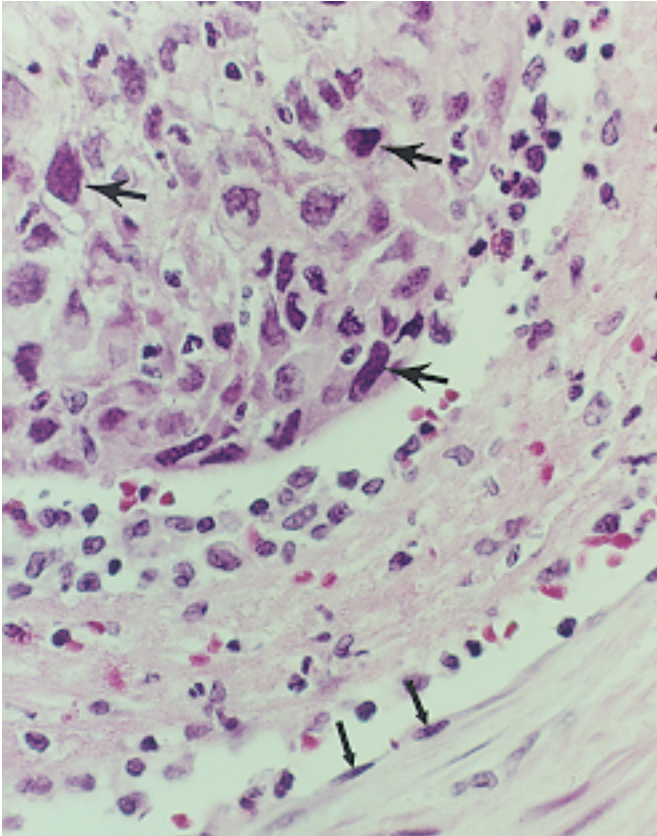
Squamous cell carcinoma, buccal; marked formation of "whorls" of malignant squamous cells, some with a tiny keratin pearl at the center (arrow). Inflammatory response is seen between the whorls.

Squamous cell carcinoma, oral cavity, graded overall as moderately differentiated showing a small keratin pearl (large arrow) in a nest of pleomorphic cells and illustrating the infiltrating character of squamous cell carcinoma with individual cells and small nests of cells separating muscle fibers (small arrows).

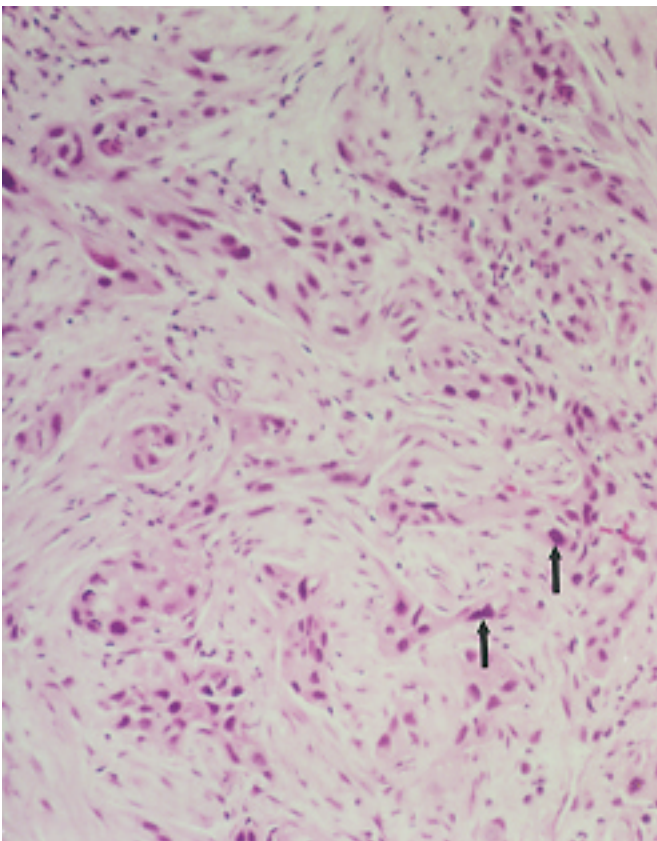


Squamous cell carcinoma, tongue. Nest of tumor cells, probably in lymphatics, surrounded by fat and the characteristic fascicles of tongue muscle that run in different planes.





Squamous cell carcinoma, epiglottis, poorly differentiated, filling a vascular channel. Note pleomorphism (large arrows) and hyperchromicity. Endothelium marked by small arrows.



Squamous cell carcinoma, nonkeratinizing infiltrating in a pattern of individual cells and small nests. Graded moderately differentiated. Nuclear pleomorphism evident (arrows).

CLINICAL ASPECTS

Laryngeal squamous cell carcinoma. Clinically, the larynx is divided into three components, supraglottic, glottic, and subglottic. The supraglottic component extends from the tip of the epiglottis and the aryepiglottic folds to the upper margin of the true vocal cord or just beneath the laryngeal ventricle; the glottic area from the upper border of the true cord to one centimeter below the lower margin of the supraglottic larynx; the subglottic area reaches downward to the lower edge of the cricoid cartilage.

Supraglottic carcinoma is usually ulcerated, fungating and bulky and the margins seem to push. The most difficult area of the supraglottic larynx in which to detect a small carcinoma is along its laryngeal surface just above the anterior commissure of the larynx since the superior aspect of the epiglottis tends to hide this portion. Any laryngoscopic examination that does not clearly demonstrate both surfaces of the epiglottis as well as the entire lengths of the vocal cords is inadequate. Carcinoma of the epiglottis eventually extends upward to invade the tongue base and in some cases may grow downward to reach the glottis (transglottic carcinoma). Many authorities believe it more likely that transglottic carcinoma originates inferiorly with the carcinoma crossing the glottic area upward to the epiglottis.

Supraglottic carcinoma is prone to metastasize earlier than glottic carcinoma probably because of more abundant lymphatic supply and because the epiglottis readily permits extension to the pre-epiglottic space. Treatment is preferably by supraglottic laryngectomy and often unilateral or bilateral neck dissection, either radical or conservative depending in the particular case and the surgeon's experience.

When there is recurrence, it almost always occurs at the superior surgical margin (tongue muscle) rather than inferiorly at the level of the true vocal cord even though only a minimal margin of normal tissue can be left inferiorly in most cases. The reason is that inferiorly the distinction between normal and abnormal is clear whereas in the superior area where tongue muscle is divided, planes are vague and cancer may easily go undetected by the surgeon.

Glottic carcinoma is the most common of laryngeal carcinomas accounting for well over fifty percent of these tumors. They almost invariably arise from the anterior one half of the vocal cord, and if the surgeon receives a pathologist's report of squamous carcinoma from a lesion situated at the posterior commissure or posterior half of the vocal cord, he should be skeptical. Since only a minute alteration of the mucosa of the true vocal cord produces hoarseness and, if the patient then has an adequate laryngeal examination, an early diagnosis of carcinoma is possible. Later, the tumor

grows to the anterior commissure and crosses to the opposite cord, or fixes one or even both vocal cords by deep muscular invasion. About 25 percent of cases with a fixed cord will have cervical metastatic disease.

Treatment of glottic carcinoma varies depending on the extent of the disease. In early cases with only carcinoma-in-situ or minimal invasive disease, a cure may be had with transoral surgical methods such as vocal cord stripping or laser evaporation. Partial laryngectomy (cordectomy) is a highly effective treatment for a patient with a mobile cord and unilateral involvement, but when the cord is fixed, total laryngectomy with or without neck dissection is recommended.

More and more, reliance is placed on definitive diagnosis by frozen section examination at the time of initial biopsy, but if this routine is followed, it must be used with great caution else sooner or later a patient without invasive carcinoma will lose his larynx.

Infraglottic carcinoma is uncommon except as it may be part of a pre-existing glottic lesion that spreads inferiorly. The usual recommended treatment is total laryngectomy and unilateral neck dissection with great attention given to paratracheal nodes that may have been clinically undemonstrable.

Irradiation therapy plays an important role in all types and stages of laryngeal carcinoma, and as a matter of fact, may be the treatment of choice in early glottic disease since it leaves the patient with a better voice than does a surgical procedure and may be just as effective.