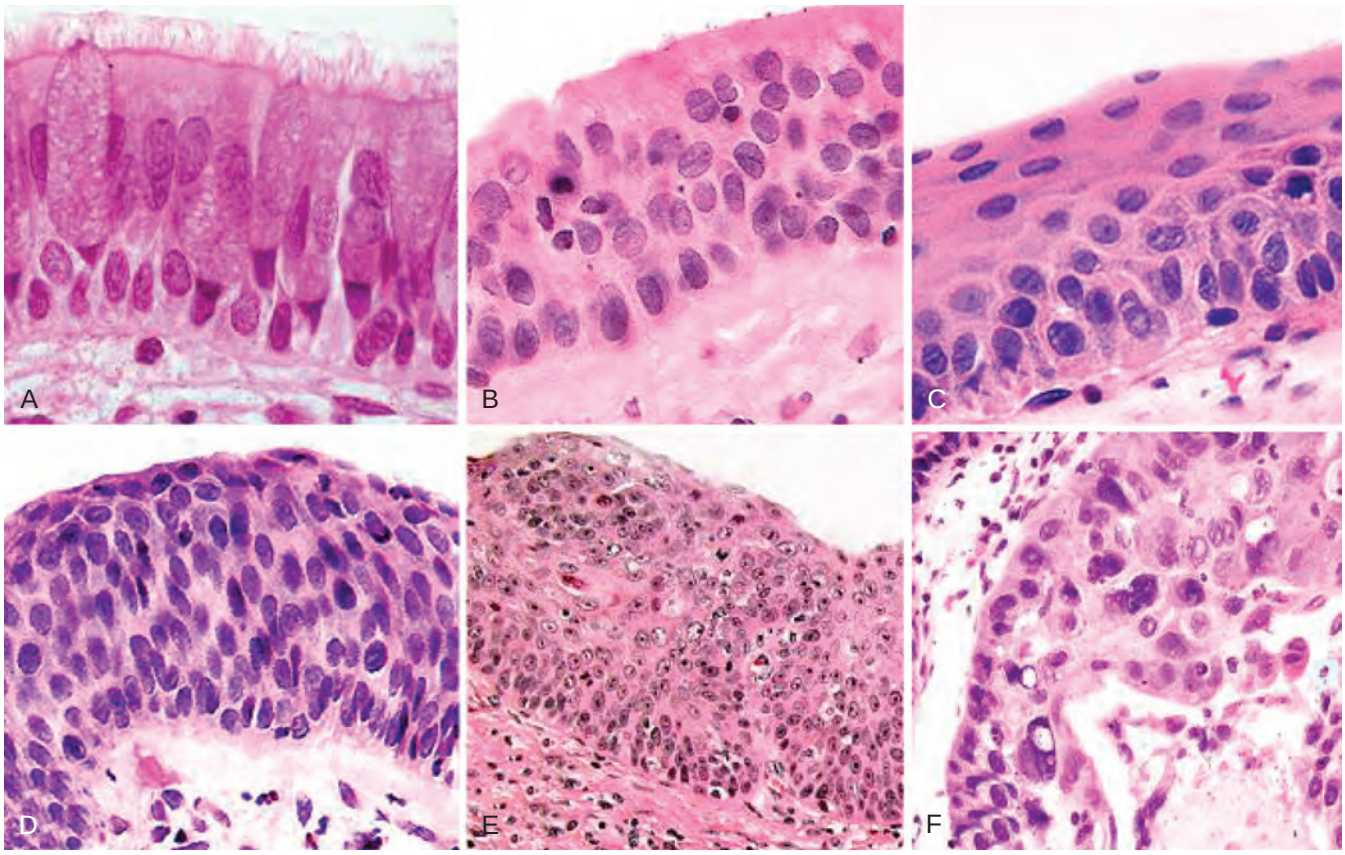

Figure 15-44 Precursor lesions of squamous cell carcinomas. Some of the earliest ("mild") changes in smoking-damaged respiratory epithelium include goblet cell hyperplasia **(A),** basal cell (or reserve cell) hyperplasia **(B),** and squamous metaplasia **(C).** More ominous changes include the appearance of squamous dysplasia **(D),** characterized by the presence of disordered squamous epithelium, with loss of nuclear polarity, nuclear hyperchromasia, pleomorphism, and mitotic figures. Squamous dysplasia may progress through the stages of mild, moderate, and severe dysplasia. Carcinoma-in-situ (CIS) **(E)**, the stage immediately preceding invasive squamous carcinoma **(F)**, by definition has not penetrated the basement membrane and has cytologic features similar to those in frank carcinoma. (**A-E,** Courtesy Dr. Adi Gazdar, Department of Pathology, University of Texas, Southwestern Medical School, Dallas. **F,** Reproduced with permission from Travis WD, et al [eds]: World Health Organization Histological Typing of Lung and Pleural Tumors. Heidelberg, Springer, 1999.)

resembling other papillary carcinomas to solid masses with only occasional mucin-producing glands and cells. The majority express thyroid transcription factor-1 (Fig 15-43*A* inset); first identified in the thyroid, this factor is required for normal lung development. At the periphery of the tumor there is often a lepidic pattern of spread, in which the tumor cells "crawl" along normal-appearing alveolar septae. Tumors (≤3 cm) with a small invasive component (≤5 mm) associated with scarring and a peripheral lepidic growth pattern are called **microinvasive adenocarcinoma**. These have a far better outcome than invasive carcinomas of the same size. **Mucinous adenocarcinomas** tend to spread aerogenously, forming satellite tumors. These may present as a solitary nodule or as multiple nodules, or an entire lobe may be consolidated by tumor, resembling lobar pneumonia and thus are less likely to be cured by surgery.

Squamous cell carcinoma is most commonly found in men and is **s**trongly associated with smoking. Precursors lesions that give rise to invasive squamous cell carcinoma are well characterized. Squamous cell carcinomas are often antedated by **squamous metaplasia** or **dysplasia** in the bronchial epithelium, which then transforms to **carcinoma in situ,** a phase that may last for several years (Fig. 15-44). By this time, atypical cells may be identified in cytologic smears of sputum or in bronchial lavage fluids or brushings (Fig. 15-45), although the lesion is asymptomatic and undetectable on radiographs. Eventually, an invasive squamous cell carcinoma appears. The tumor may then follow a variety of paths. It may grow exophytically into the bronchial lumen, producing an intraluminal mass. With further enlargement the bronchus becomes obstructed, leading to distal atelectasis and infection. The tumor may also penetrate the wall of the bronchus and infiltrate along the peribronchial tissue (Fig. 15-46) into the adjacent carina or mediastinum. In other instances, the tumor grows along a broad front to produce a cauliflower-like intraparenchymal mass that pushes lung substance ahead of it. As in almost all types of lung cancer, the neoplastic tissue is gray-white and firm to hard. Especially when the tumors are bulky, focal areas of hemorrhage or necrosis may appear to produce red or yellow-white mottling and softening. Sometimes these necrotic foci cavitate.

Histologically, squamous cell carcinoma is characterized by the presence of keratinization and/or intercellular bridges. Keratinization may take the form of squamous pearls or individual cells with markedly eosinophilic dense cytoplasm (Fig. 15-43*B*). These features are prominent in well-differentiated tumors, are easily seen but not extensive in moderately