9 Hyperplasia, metaplasia and carcinoma \textit{in situ}

When the tracheobronchial epithelium is damaged, mucous cells and basal cells proliferate in response to the injury. Mucous cells appear to play the dominant proliferative role and, resulting from a marked increase in their mitotic rate, pathological lesions are produced which include 'goblet' cell hyperplasia, stratification and noncornifying and cornifying epidermoid (squamous) metaplasias. These lesions, although morphologically dissimilar, are brought about by the wide and varied spectrum of phenotypic expression of mucous cells. Depending on the nature and extent of the injury, one or more of these lesions may be expressed simultaneously in the same specimen, and one lesion may change into another.

The epithelium demonstrates a stereotyped response to diverse forms of injury. For example, epidermoid metaplasia occurs in man and animals in response to a variety of insults including mechanical and nutritional injuries (vitamin A deficiency), radiation injury, irritant gases, infectious agents and carcinogens, to name but a few (Francis and Stuart-Harris, 1938; Wong and Buck, 1971; Harris \textit{et al.}, 1972; Asmundsson \textit{et al.}, 1973; Nettesheim, 1976; Nettesheim and Griesemer, 1978; McDowell \textit{et al.}, 1979; Wilson \textit{et al.}, 1984). Moreover, combined epidermoid (well-developed keratin tonofilaments) and secretory specializations (mucous granules) are characteristic of the cells of these lesions irrespective of the cause.

When the insult and adverse environment are removed, the metaplastic lesions may reverse. Experiments in hamsters have shown that division of mucous cells, both metaplastic and normal columnar forms, provide for columnar mucous and preciliated cell progeny which restore the mucociliary state (Keenan \textit{et al.}, 1982a, b, c, 1983). However, if the epithelial cells have been exposed to an initiating dose of carcinogen and promoting factors, lesions may progress towards carcinoma \textit{in situ}, which in turn may lead to invasive carcinoma.

A working hypothesis will be developed throughout this chapter which emphasizes the pivotal role of mucous cells in the development, maintenance, and regeneration of the neoplastic state (Scheme 9.1). This hypothesis has been presented in more detail elsewhere (McDowell and Trump, 1983).
Scheme 9.1 Development, maintenance, regeneration and neoplasia of the mucociliary tracheobronchial epithelium: a working hypothesis.

- **Mucous cell hyperplasia** is a late change in vitamin A deficiency, associated with death and sloughing of epithelial cells.
- **Initiation and promotion** may act on columnar and/or polygonal mucous cells.
- **X** Mitotic division(s).