The mast cell was first described by Paul Ehrlich in 1876, as a tissue fixed cell containing many granules which exhibited metachromasia when exposed to basic dyes such as toluidine blue. This histochemical characteristic indicates the presence of the highly acidic proteoglycan, heparin, one of the many preformed chemical mast cell mediators which are secreted in response to cell activation. At the turn of the century, the structural elucidation of histamine (Windaus and Vogt 1907), its association with the mast cell (Best et al. 1927) and its release following anaphylactic reactions in animal models (Dale 1910) established a role for the mast cell in mediating the type I or immediate hypersensitivity response associated with allergic reactions. This type of immunological reaction has been implicated in the pathogenesis of skin diseases such as eczema and urticaria. Indeed, the skin has been used as the primary site at which to undertake allergen testing, in the form of intradermal or prick tests, and into which allergens may be introduced in hyposensitisation treatment. Apart from the immediate hypersensitivity reaction involving the reaginic antibody IgE, mast cells play a contributory role in the defence against neoplasia (Goto et al. 1984), in regulating fibroblast growth and maturation (Gupta 1970; Kawanami et al. 1985) and in the elimination of nematode parasites (Wells 1977). The recognition of a wider role for the mast cell in the pathogenesis of human disease has stimulated renewed interest in this cell. As in the gastrointestinal and respiratory tracts, the potential importance of mast cells in human skin is reflected by the large numbers that are present in this tissue. Because of the relative inaccessibility of tissue mast cells, much of the knowledge that has been gained about mast cell structure and function has been derived from studies of rat peritoneal mast cells, which can be recovered in large numbers and purified to homogeneity. Recently, however, the use of a variety of enzyme digestion techniques has enabled mast cells from other sources to be dispersed. These techniques have provided overwhelming evidence that mast cells from different species, and even from different sites within the same species, exhibit heterogeneity with respect to both structure and function (Church et al. 1982; Benyon et al. 1987; Lowman et al. 1987). Conclusions drawn from studies of mast cells of one particular animal or body site may not, therefore, be applicable to mast cells of another species or site.

In this chapter, we discuss the morphology, distribution, structure and possible functions of human mast cells, particularly those of human skin, and compare them with those of the more widely studied rodent mast cells.
A. Mast Cell Content of Human Skin

The number of mast cells in human skin has been the subject of conflicting reports. MIKHAIL and MILLER-MILINSKA (1964), using toluidine blue to stain mast cells in human skin, found approximately $7 \times 10^3$ mast cells/mm$^3$ with no significant variation in relation to age, sex, race or body region. This is in marked contrast to earlier studies by HELLSTROM and HOLMGREN (1950), who showed $7 \times 10^3$ mast cells/mm$^3$ in the corium of newborn babies but only $1 \times 10^3$ mast cells/mm$^3$ in the same sites of 70- to 80-year-old subjects. Furthermore, BINAZZI and RAM-PICHINI (1959) showed considerable variation in the mast cell populations from area to area in human skin, ranging from 46 mast cells/mm$^3$ in skin from the leg to 177 mast cells/mm$^3$ in the scrotal skin.

Under normal conditions, mast cells are not found in the epidermis of healthy skin, though they move into this site during various disease states. Mast cells in the dermis are not randomly distributed but are grouped around blood vessels, nerves and appendages (EADY et al. 1979). Using a careful mapping technique to define more precisely the distribution of mast cells within human skin, COWEN et al. (1979) showed that in skin biopsy specimens from the forearm and upper arm, the greatest density of mast cells occurred in the superficial dermal zone just below the dermo-epidermal junction. A close correlation has been found between mast cell numbers and histamine content of human skin (EADY et al. 1979), though extreme methods have proven necessary to ensure that all the histamine was extracted from the skin. Using repeated boiling to extract histamine from the tissue, SONDERGAARD and ZACHARIAE (1968) found significant amounts of this mediator in the epidermis of human skin, a site which is histologically devoid of mast cells. With the recognition that both rodent and human tissues may contain atypical mast cells which require special fixation procedures for their visualisation (ENERBACK 1966a; STROBEL et al. 1981), it can be concluded that the discrepancies in histamine content and mast cell numbers at various sites in human skin may not necessarily indicate a non-mast cell source of histamine; rather there may be mast cells or mast cell precursors in human skin which cannot be visualised with metachromatic stains. Alternatively, the presence of epidermal histamine may represent the uptake of mast cell granules or histamine by phagocytic cells in this skin layer.

B. Mast Cell Structure

The metachromasia of mast cell granules exhibited on binding of basic dyes has meant that the light microscopic appearance of the cells has been well described. Mast cells located in the corium are about 5–15 μm in length, though occasionally cells as large as 30 μm have been reported. Their shape has been variously described as polyhedral, fusiform, ovoid, rectangular and rectangular, with a cytoplasm containing a variable number of lysosomal granules 0.1–0.5 μm in diameter. When free from the constraints of the surrounding tissue elements, dispersed skin mast cells are rounded; this allows more accurate size estimates to be made, and according to BENYON et al. (1987) the cells are 4–18 μm in diameter, with 79%