INTRODUCTION

The sebaceous gland is a universal attribute of mammals which does not occur in amphibians and reptiles and the only analogous structure found in birds is the comparatively huge preen gland on the rump. Some of the cutaneous glands of amphibia and the crocodilia, which have a casual resemblance to sebaceous glands, are different organs. Some cutaneous glands of reptiles, however, are considered to be phylogenetic fore-runners of mammalian sebaceous glands, such as the femoral glands of lizards, the cloacal glands of crocodiles and the anal glands of turtles and giant serpents (Schaffer, 1930).

Although basically similar, sebaceous glands of different mammals show many differences in form and distribution. Some mammals such as true lemurs have numerous sebaceous glands whereas the whales and porpoises have virtually none; except in the external auditory meatus and over the genitalia. The glands may be small and simple as in ornithorhynchus, the mouse,

the insectivora and some of the Prosimii or they may be large and complex as in the bats and lemurs (Montagna, 1963). Sebaceous glands are wide-spread over the human body, though not normally found on the palms or soles, and only sparsely on the dorsum of the hand and foot (Johnsen and Kirk, 1952). Sebaceous glands are largest and most numerous in the midline on the back, on the forehead and face, in the external auditory meatus and on the anogenital surfaces (Ebling, 1977). Sebaceous glands normally, though not invariably, develop in association with hair follicles and open into pilary canals, except in the lemurs, where they open directly onto the surface of the skin. In addition to their general distribution in varying densities all over the body most mammals have some specialized glands which are not associated with hair follicles, and may have beem shown to be concerned with production of scent or pheromones. Marmosets, tamarians and shrews have a large field of abdominal sebaceous glands and tarsiers have huge labial glands. In Felidae and Canidae anal sacs contain many large sebaceous glands. Several species of bats, pigs and others have large single or multiple

intermandibular sebaceous glands in the gular region. The meibomian glands in the palpebrae are specialized sebaceous glands. Most primates, including man, have extensive fields of free sebaceous glands around the anogenital surface (Montagna, 1963). Some of the modified sebaceous glands viz., preputial glands of rodents, the supracaudal gland of the guinea pig, inguinal glands of rabbits and costovertebral glands of hamsters, are easily amenable to surgical isolation for experimentation by virtue of their larger size. In contrast to gross morphological variations the histology of sebaceous glands is largely similar, but not necessarily identical, in all mammals.

Preputial glands of rodents are a pair of flask shaped specialized glands of sebaceous type, rather gigantic in size for their category, which open by respective single ducts alongside the urethral orifice. These glands are lipid secreting organs. Preputial secretion of rodents is known to contain pheromonic substance(s) working as sex attractant drawing the conspecific together, whereupon various kinds of social

interactions may occur; including courtship and mating. Such possibilities have attracted the attention of ethologists(Bronson and Caroom, 1971; Orsulak and Gawienowski, 1972). The preputial glands have also attracted attention of several research workers from another biological discipline namely dermatology. The present attempt to study certain aspects of the histo-physiology of this gland aims at a general enlightenment regarding its functional significance in the life of rodents.

Sebaceous differentiation is a complex and serial process of orderly synthesis, segregation and accumulation of lipid droplets culminating in enlarged, mis-shapen cells that fragment to form the sebum and the glands are, thus, said to be holocrine.

More than a decade of investigations have established beyond doubt that the development and secretory activity of the sebaceous glands of man, and those of other mammals are strikingly influenced by hormonal factors, (Ebling, 1974; Shuster and Thody; 1974;

Pochi and Strauss, 1974). Most investigators have taken the size of glands and the incidence of mitosis as criteria of activity. Numerous studies have established the dependence of sebaceous gland development and functioning on androgens. Ebling (1963) has reviewed widespread reports on the effect of castration leading to atrophy of the sebaceous glands. Thody and Shuster (1970 a,b) and Strauss and Pochi (1963) have also shown that sebum production is decreased following castration. Moreover Pochi et al. (1962) have suggested, on basis of their observations on sebaceous gland secretion in castrated males, that the adrenal gland too, is important for the functioning of the sebaceous gland, and that the sebaceous gland does not depend entirely upon gonadal androgens but adrenal androgens may also contribute significantly in this regard (Pochi and Strauss, 1974). However, at the outset, it should be stressed that the exact role and interplay of hormones on enzymes concerned with synthesis of sebaceous gland lipids have not yet been fully elucidated. Although, most investigators have studied rate of sebum

secretion of sebaceous glands due to changes in hormonal environment, quantitative and/or qualitative data regarding the biochemical changes concerned with lipid synthesis are lacking. Therefore, examination of total lipid content of the gland and the estimations of the glucose-6-phosphate dehydrogenase and 'malic' enzyme' which provide the source of reductive hydrogen for fatty acid synthesis were taken up (Chapter-1).

Preputial gland cells have an adequate blood supply, and hence, supply of glucose is not a limiting factor in the gland. Moreover, active glucose catabolism (glycolysis and Krebs' cycle) can provide additional ATP ~~mols~~ alongwith acetyl Co A, reducing equivalents and precursors like glycerophosphate necessary for lipogenesis in the gland. A histoenzymological study of α-glycerophosphate dehydrogenase and other oxidative enzymes in normal, castrated and adrenalectomized-castrated animals (Chapter-2) would contribute to an understanding of metabolic control of the preputial gland and its dependence on androgens; either gonadal or of adrenal in origin.

Sansone and Reisner (1974) have reported that the sebaceous glands themselves participate meaningfully in controlling their own tissue specific stimulators and inhibitors rather than acting as passive recipients of such regulators brought to them through circulation. A number of investigators have examined the *in vitro* metabolism of androgens in various sebaceous gland analogues (Wilson and Gloyna, 1970; Bardin *et al.*,1970; Bullock *et al.*,1970; Richardson and Axelrod, 1971). Balogh (1966) and Muir *et al.* (1970) have reported the histochemical localization of hydroxysteroid dehydrogenases (HSDHs) in the preputial gland. It is apparent that HSDHs are important for metabolic interconversions of steroids. However, these enzymes have not been studied in the preputial glands of androgen-deprived rats. In order to get some idea about steroid metabolism in various cell types of the gland; histoenzymological studies of HSDHs were carried out in the preputial glands of normal, castrated and adrenalectomized-castrated rats (Chapter-3).

The autolytic process of sebaceous secretion has been investigated in rat sebaceous glands by Brandes

et al. (1965). Lazarus et al. (1975) suggested that lysosomal proliferation and subsequent rupture plays a primary role in the programmed autolysis, which is the characteristic feature of the holocrine secretory glands. Acid phosphatase is a lysosomal enzyme and can be considered as an index of lysosomal activity. Montagna and Hamilton (1947) have reported high acid phosphatase activity in hamster sebaceous glands. Many investigators (Gutman and Gutman, 1938; Howard and Robert, 1952; Sansone et al., 1972) have reported high acid phosphatase activity in the preputiel glands. Androgens are known to reduce the rate of sebum secretion. In order to know whether such effects occur due to reduction in the rate of sebum synthesis and/or through decrease in autolytic process, effects of castration and adrenalectomy on the phosphatase activity levels in the glands were studied (Chapter-6).

Much has been said about the biochemistry and hormonal control of sebaceous secretion. The histological and histochemical characteristics of sebaceous glands and influences of androgens on them have been well

documented in the literature. However, the problem of sebaceous gland innervation and its possible significance is full of disputes, contradictions and confusions. The interplay of hormones and neural components on physiology of the gland remains to be established. Neurohistological studies have yielded no decisive evidences on secretory innervation of the sebaceous glands. Rothman (1954) reviewed the problem of innervation of sebaceous glands. Winkelmann(1960) failed to demonstrate any autonomous nerve supply to the sebaceous glands. Montagna (1963) also favoured the view that there are no nerves to the sebaceous glands. To scrutinize the problem further, innervation of the preputial glands was studied by employing histological, histochemical and pharmacological techniques (Chapter-4).

There are no conclusive experimental evidences to show that the gland is directly under the control of autonomic nervous system. The action of nerves is effected through chemical mediators and these can easily be simulated by administration of suitable agonistic drugs. To analyse the relative contribution

of sympathomimetic and parasympathomimetic agents towards the functioning of the gland; adrenergic and cholinergic agonists were administered and the effects were studied. Further, to characterize the mediatory influence of adrenergic receptors on the mechanism of extrusion of preformed sebum from the gland an experiment was conducted to study in vitro effects of α and β adrenergic agonists and antagonists (Chapter-5).

As mentioned earlier, sebaceous glands of general body skin and some of the specialized glands are androgen dependent and they decrease in size when the sources of androgen are depleted. However, the effects of adrenergic agonists on histological structure of the gland are not known. In a holocrine secretory gland, size of the gland depends on renewal of cells (mitoses), and cellular disintegration, which can be judged by studying a lysosomal enzyme like acid phosphatase. β -adrenergic agonists are reported to decrease mitosis in normal and psoriatic skin (Voorhees et al., 1975). To investigate the possible role of adrenergic and cholinergic agonists on the gland,

histomorphometric changes (Chapter-7) and levels of nonspecific phosphatases of the gland (Chapter-4) were studied.

After studying the influence of adrenergic agonists on the functional activity of this gland, the next logical problem to be considered is whether these agonists influence the gland directly or they alter the steroid metabolism of the gland. The gland is androgen dependent and changes in the metabolism or interconversions of the steroids caused by adrenergic agonist are likely to alter the functional patterns of the gland. The study of hydroxysteroid dehydrogenases to be described in Chapter-8 is aimed at elucidation of possible influences of the adrenergic agonists (isoproterenol) on the steroid metabolism of the gland.