BIOLOGY

Irreversible Cellular Changes in Old Mice

CELLULAR changes accompanying ageing are known to occur in a number of organs, for example, liver[1], bile ducts[2], pancreas[3], thyroid[4] and prostate[5], and may be due to an intrinsic change in the tissue cells or to humoral changes in the host. Most of this work, however, is based on histological investigations of fixed material and little is known about the biological potential of these tissues. In a preliminary investigation[5] the response to hormones of prostatic tissue from young (1·5 months), adult (4–5 months) and old (24 months) mice was investigated in organ cultures and differences in reaction were described. The prostates of the old mice also showed a general epithelial atrophy, but with areas of giant cells and presumed hyperdiploid cells with large irregular nuclei. When these tissues were maintained *in vitro* on a medium containing normal adult human serum some of these changes regressed, but the cultures were maintained for a relatively short time (21 days). To investigate the effects of the humoral environment on tissues of different ages for longer periods, a series of experiments were carried out by grafting old and young prostatic tissue into hosts of different ages. These animals can be described as age chimeras[6].

*C*57 black mice were used in all experiments. The ventral prostates were removed from the donor animals and each lobe of the paired gland dissected to free the tubules and divided into two parts. These were transplanted subcutaneously into the flank of the host mice with a modified Bashford-type needle. Animals from each group were killed at intervals from 4–539 days, and the grafts and the hosts' ventral prostates examined. The number of transplants and the ages of donors and hosts are given in Table 1.

Table 1. AGE OF DONORS AND HOSTS

Age of donors (months)	No. of transplants	Age of hosts (months)
1·5	42	3–5
5	60	5
8	6	8
24	48	3–5

All the grafts retained their normal structure, although some acini became distended with secretion. As in the intact prostate, the epithelium in the distended acini was lower than that in the smaller glands. Grafts from the young and adult animals did not differ as a rule from the prostates in the host animals. In the early stages of the experiment the prostatic epithelium in both was normal (Fig. 1). After 500 days, however, 'hyperdiploid' cells were present. These were more frequent in the grafts from the 8 months old mice than in hosts of the same age, but only 2 of these animals survived for this period. The transplants from the 24 months old animals also contained cystic acini with low epithelium, but in the smaller glands the epithelium was very tall and foamy and resembled that seen in testosterone-treated animals; mitoses were seen in these cells. The giant cells and presumed hyperdiploid cells remained unchanged (Fig. 2). These findings in the old grafts were present at 31 days, when the first animals were killed. The host prostates from animals bearing the old grafts were all normal.

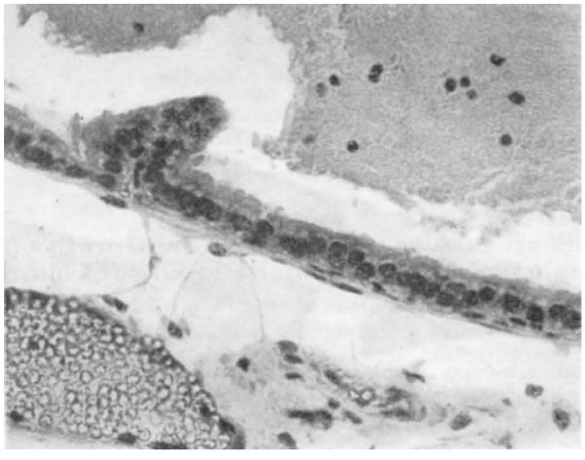

Fig. 1. Graft (62 days) from 1·5 months old donor showing normal epithelium (hæmatoxylin and eosin. × *c.* 430)

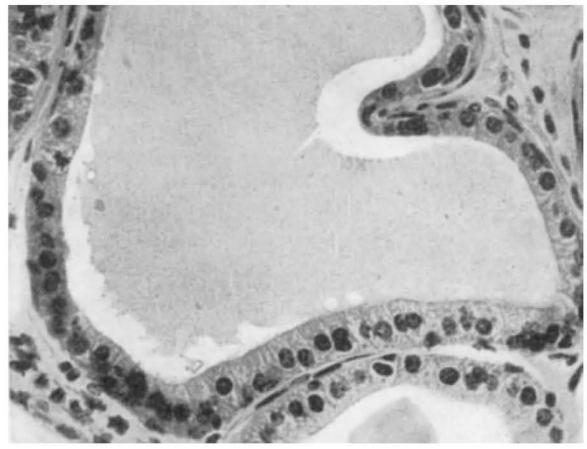

Fig. 2. Graft (104 days) from 24 months old donor showing tall foamy epithelium, 'hyperdiploid' cells in papilla and cell in mitosis (hæmatoxylin and eosin. × *c.* 430)

These experiments confirm the *in vitro* finding that the epithelial atrophy is reversible and is presumably due to humoral changes, perhaps an androgen deficiency in the old mice. There are also differences in the cells themselves in the old tissues. First, mitoses are found in the epithelial cells in the old grafts although they are uncommon in young tissue either in grafts or in the intact prostate. Secondly, the 'hyperdiploid' cells with giant nuclei persist. Last, as in the organ cultures, the secretory response of the old tissue differs from that of the young tissue, but *in vivo* the old epithelium reacts more strongly whereas *in vitro* it appears to be less responsive. This may be due to deficiencies in the tissue culture medium. These cellular changes seem to be irreversible.

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Ultra-structure of Carotid Body Tissue as seen in Serial Sections

THE ultra-structure and hence the mode of functioning of the alleged chemoreceptors of the carotid body are still the least understood of all known sensory tissues. In a previous investigation it was pointed out that further knowledge would depend on three-dimensional pictures, such as can be obtained by the use of serial sections[1].

The present observations are based on six series of electron microscope sections of cat carotid body, fixed with Palade's fixative, embedded in 'Epon' or methacrylate and stained with uranyl acetate. A survey of the