LETTERS TO THE EDITORS

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Attenuation of Host Reaction to Ovarian Homografts

GRAFTS derived from ovarian tissue which has been treated with glycerol and frozen to, and stored at, − 79° C. are endocrinologically active but contain comparatively few oocytes[1]. The oocytes which survive freezing and thawing can mature and undergo ovulation even in subcutaneous grafts[2]; but it is not yet known whether they are capable of normal fertilization and development. An approach to this problem involves orthotopic grafting at the ovarian site of the ovariectomized or sterilized recipient and, ideally, the use of a graft from a genetically distinguishable donor so that the source of any offspring produced is not in doubt. With the animals at present available at this Institute the latter requirement implies interstrain ovarian homografting and has led us to consider possible methods of attenuating or suspending the immunological reaction evoked by such grafts.

Several different procedures have been found to modify host reaction to homografts of various kinds[3]. The most attractive one from the present point of view is based on the observation that the growth of certain homologous grafts is enhanced by the previous intraperitoneal injection of the host with suspension of killed tissue of the same genetic composition as the prospective graft. This effect of such pretreatment, discovered and extensively studied in relation to tumour tissue[4], was not found by Kaliss and Spain[5] to occur with normal tissues; but Billingham, Brent and Medawar[6] have recently reported slight prolongation of survival of skin homografts following the pretreatment of the host with lyophilized tissue from the donor strain.

Two strains of rats, albino and hooded, are available at this Institute. With both of these, intrastrain ovarian homografts take and persist readily, while interstrain homografts are frequently accepted but persist less readily[7]. In particular, ovarian tissue from 'hooded' donors grafted into albino hosts usually ceases to function within a month, and this combination was therefore chosen for work on pretreating the recipients.

Ovaries of the hooded strain were homogenized in Ringer solution, frozen and thawed, once or repeatedly, and the suspension injected intraperitoneally. In an early experiment a suspension equivalent to a total of five pairs of ovaries was given to each albino recipient on days 14, 13, 12 and 4 before grafts were made from hooded donors. After 28 days, the grafts were still functioning in 7–10 of the pretreated recipients as compared with 7–27 of untreated but otherwise similar recipients for which records were available at the time. Afterwards, pretreatment was by a single intraperitoneal injection equivalent to four pairs of ovaries, groups of ten pretreated recipients and ten untreated recipients being used for each test. The first variable examined was the time of treatment before grafting, intervals of 1, 3 and 7 days being chosen in the light of the work of Kaliss and Day[8] on tumour grafts. Suggestive results were obtained with the recipients treated 7 days before the grafts were made, and three replications of this experiment were therefore carried out. In each, more grafts took and many more persisted in pretreated than in untreated recipients. The final result was that the grafts became active in 20–39 of the untreated recipients and remained active for 28 days or more in 7–39, the corresponding figures for the pretreated recipients being 31–40 and 24–40. The difference at 28 days is highly significant ($p = 0{\cdot}001$) and leaves little doubt that the pretreatment had had a significant effect upon the survival of the graft. The effect may be prolonged as continued observation in the first two experiments showed that active grafts were present in 0–20 untreated and 9–20 treated recipients at three months after grafting. Further experiments suggest that freezing of the suspension is not necessary, except perhaps to prevent the formation of ancillary grafts on the peritoneum. Suspensions subjected to ultrasonic vibrations are equally or even more effective. Work with other tissues and on component parts of the suspension is in progress, with the view of applying the technique to the extension and development of orthotopic ovarian grafting and the study of oocyte survival in frozen and stored tissue.

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Corneal Homografts

IT has now been established that homografts of cornea and cartilage behave quite differently from skin homografts and can survive for long periods. The clinical success of the corneal graft has been known since 1878[1], and there is ample evidence from histological and autoradiographic studies of experimental corneal homografts to confirm that they remain viable long after homografts of tissues such as skin are destroyed by the host tissues[2–4].

We have now examined more than a hundred corneal homografts implanted subcutaneously into guinea pigs and have found preservation of the corneal epithelium after two months, while at the end of three months the ground-substance survives unvascularized.

Experiments have recently been completed to test for any host sensitization. In fifteen guinea pigs a corneal homograft was inserted into the left lateral body wall, and four weeks later a second corneal homograft from the same donor was placed in a corresponding position on the right side of each animal and the grafts left in position for a further two weeks. Twenty-four hours before removal of the grafts the host animal was given 5 mc. of sulphur-

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