Conditions which eliminate Inflammation to Homografts in Rabbits

The stimulus for production of a sterile cellular infiltrate, principally lymphocytic, in and about a homograft remains obscure. Methods whereby this inflammatory reaction may be eliminated are worthy of consideration with the view of successful homografting between members of genetically impure strains.

Previous studies using musculofascial transplants of erector spinæ of rabbits permitted accurate distinctions to be made by ordinary histological methods between autografts and homografts[1]. Microscopic examination two weeks after implantation showed that both types of grafts underwent similar sequences of degeneration, resorption and organization, but in the homograft inflammation was superimposed upon the repairative matrix of the musculofascial zone. Angiitis involving the newly formed channels was a frequent feature of the inflammatory reaction.

Further experiments have shown that the classical inflammatory aspects of host–homograft interactions may be eliminated by several conditions. One condition was by reduction of 'viability' of tissues of the musculofascial graft by exposure to extremes of heat, cold or X-irradiation prior to implantation[2,3]. Both types of grafts so treated elicited a sluggish fibro-collagenous response by the host. Grafts studied following less extreme exposure to temperature and X-irradiation showed that the degree of admixture of proliferating cells of the graft with those of the host seemed to determine the magnitude of the inflammatory reaction in homografts.

A second condition for the elimination of inflammation in homografts required grafting between parabionts in the post-parabiotic period. Rabbits surgically united by the ears developed a cross-circulation lasting between 7 and 13 days after anastomosis[4]. The cessation of the cross-circulation seemed to be related to the development of inflammation at the surgical plane of anastomosis between the animals. Joining rabbit parabionts a second time failed to reproduce sequences of healing noted at primary junctions. This was in accord with the "second set rejection phenomenon"[5]. Microscopic study of cross-homografts between parabiotic partners following one and two periods of parabiosis showed two types of tissue reaction equally distributed between the two groups of parabionts[6]. The first type consisted of a fibro-collagenous encapsulation of the graft by the host in the absence of vascular penetration. Inflammation did not develop. The second type of post-parabiotic modification was similar to the first, with the exception that a peculiar angiomatous vascular plexus of capillaries arising from the host grew beneath the fascia of the homograft. Inflammation was again absent.

The third condition required cross-transfusion. Since a transient cross-circulation was a conspicuous feature of the primary healing between parabionts, cross-transfusions of whole blood, controlled in quantity, were done between pairs of rabbits[7]. This eliminated all factors involved in parabiosis except exchange of blood. The microscopic study of cross-homografts following cross-transfusions showed a vascularizing stromal penetration identical to the second type of host–homograft interaction following parabiosis. Inflammation was absent.

A fourth condition required for elimination of inflammation in homografts was the pregnant state. Gravid rabbits (13–15 days of gestation) were cross-grafted with males and non-pregnant females of the same species[8]. Autografts were also implanted. Each pregnant host reacted in the same way to autografts and homografts. Both types of grafts showed the usual sequences of degeneration, absorption and organization in the absence of inflammation characteristic of host–autograft reactions. It appeared that pregnancy lessened the capacity of the animal to react against grafts of normal homologous tissues.

These observations have indicated that investigation of the means by which the inflammatory aspects of host–homograft interactions are eliminated may offer clues to the solution of the problem of successful homografting.

This work has received generous support from the National Heart Institute (*H*-1630, *H*-3215), National Institutes of Health, United States Public Health Service; the Muscular Dystrophy Associations of America, Inc., and the Otho S.A. Sprague Memorial Institute.

Richard H. Andresen
Clarence W. Monroe
George M. Hass
Dorothy A. Madden

Department of Pathology and
Laboratory of Surgical Research,
Presbyterian-St. Luke's Hospital,
Chicago.
Aug. 20.

1 Andresen, R. H., Monroe, C. W., and Hass, G. M., *J. Exp. Med.*, **95**, 509 (1952).
2 Andresen, R. H., Monroe, C. W., Hass, G. M., and Madden, D. A., *A.M.A. Arch. Path.*, **62**, 272 (1956).
3 Andresen, R. H., Monroe, C. W., Madden, D. A., Squire, F., and Hass, G. M., *A.M.A. Arch. Path.*, **58**, 455 (1954).
4 Andresen, R. H., Monroe, C. W., and Hass, G. M., *A.M.A. Arch. Path.* **58**, 455 (1954).
5 Medawar, P. B., *J. Anat.*, **78**, 176 (1944).
6 Andresen, R. H., Monroe, C. W., Hass, G. M., and Madden, D. A., *J. Exp. Med.*, **105**, 85 (1957).
7 Andresen, R. H., Monroe, C. W., Hass, G. M., and Madden, D. A. *J. Exp. Med.*, **108**, 131 (1958).
8 Andresen, R. H., Monroe, C. W., Hass, G. M., and Madden, D. A., Rep. Second World Congr., Int. Fed. Obstet. and Gynec., Montreal, 1958 (in the press).

Sarcoma in Albino Rats treated during the Embryonic Stage with Rous Virus

The cystic-hæmorrhagic disease[1,2] of albino rats caused by the Rous sarcoma virus indicates that the rats are susceptible to this virus. Starting from the well-known work of Duran-Reynals[3,4] I have attempted to reduce the susceptibility of the rats to the Rous virus by treating embryos with specific antibodies. The technique of inoculation has been described elsewhere[5].

0·1–0·15 ml. 50 per cent homogenate of the Rous sarcoma was injected subcutaneously into each embryo of four laparotomized pregnant white rats. Concurrently 0·2–0·25 ml. antiserum of rabbits repeatedly immunized with the homogenate of the Rous sarcoma was injected intraperitoneally into the same embryos. Of the four pregnant rats, two aborted, one gave birth to and suffocated its litter, and only one bore successfully five rats, of which two were suffocated.

In two of the three surviving rats small, very slowly growing cysts developed one month after the