REGENERATION OF TRANSPLANTED LYMPH GLANDS

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After autotransplantation of whole lymph glands most of the lymphocytes die; only some areas of exposed reticular stroma and small groups of lymphoid cells immediately under the capsule of the gland survive. Regeneration of the lymphoid tissue subsequently takes place in the zone of preserved stroma [1, 2, 5, 8].

We were interested to discover how the different antigenic composition of the tissues of the donor and recipient would be reflected in regeneration of the lymphoid tissue, especially after transplantation of the lymph glands of animals of the parent line into first generation (F_1) hybrids.

In the investigation described below regeneration of lymph glands was studied after iso- and homografting, and also grafting from animals of the parent line into F_1 hybrids. In the last case hybrids obtained by crossing mice of two pure lines do not reject tissues grafted on them from mice of the parent lines [3].

EXPERIMENTAL METHOD

Mice of lines A, $CBAT_6T_6$, C57BL, and $(A \times CBAT_6T_6)F_1$ aged 2-3 months were used. Purity of the lines was systematically checked by skin grafting.

Axillary, inguinal, and cubital lymph glands were grafted beneath the skin of the thorax at the rate of one gland to each recipient. Glands from female donors were grafted into males and females, but glands from males were grafted only into males. The operations were performed under Nembutal anesthesia.

The grafts were fixed in an alcohol-formalin mixture after periods of 2 h and 1, 2, 3, 5, 8, 12, 16, and 20 days, and 1.5 and 2 months.

Series of sections 5 μ in thickness were stained with hematoxylin-eosin and methyl green-pyronine. Altogether about 160 grafts were studied. Besides histologic observations, large and small lymphocytes and cells of "blast" type were counted in 200 lymphoid cells in the sections.

There were three series of experiments: series I—isografting into mice of lines A and $CBAT_6T_6$ and into $(A \times CBAT_6T_6)F_1$ hybrids; 55 grafts were studied. Series III—homografting from A into $CBAT_6T_6$ and from A into C57BL; 43 grafts were studied.

EXPERIMENTAL RESULTS

Series I-Isografting. From 2 h until the 2nd-3rd day after grafting massive death of lymphocytes took place. Only small groups of living lymphoid cells were found immediately beneath the gland capsule. These groups consisted mainly of small and medium-sized lymphocytes, although large lymphotyces and a few cells of "blast" type were present among them. The large central part of the gland was occupied by necrotic debris, consisting of a mass of disintegrating cells and nuclear material in the form of clumps of chromatin, surrounded by a light ring of exposed reticular stroma, the cells of which were still viable. Starting with the second day, and reaching its maximum on the fifth, intensive growth of blood vessels took place from the capsule into the interior of the gland.

On the 5th-8th day of lymphoid cells at the periphery of the gland had increased, and they often formed a complete rim or semicircle under the gland capsule. Mitoses were present among them, but only very few. By the 12th day resorption of the cell debris was complete, and lymphoid tissue with visible subdivision into cortex and medulla was found in the glands. The medulla consisted of light, apparently empty

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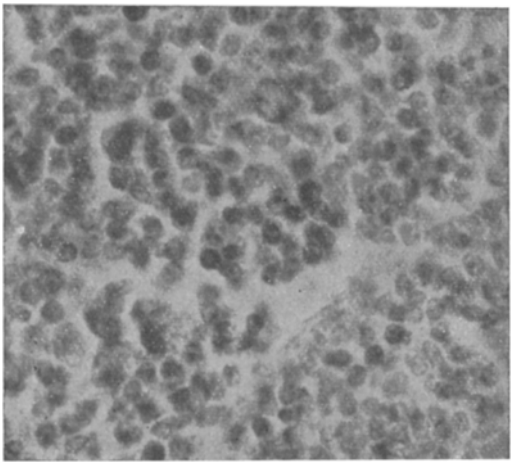

Fig. 1. Isograft of lymph gland after 20 days. Complete regeneration of lymph gland. 900 ×.

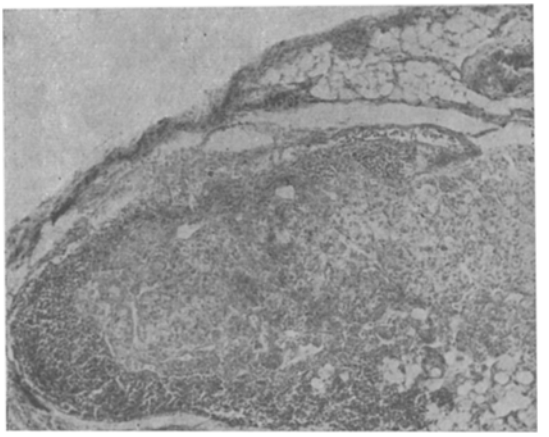

Fig. 2. Lymph gland 20 days after grafting from mouse of parent line into F_1 hybrid. Lymphoid tissue forms a semicircle at the periphery of the gland. Light reticular tissue is seen in the center. 106 ×.

bands of reticular syncytium. On the 20th day the cortex of the isografts was almost completely restored, occupying a larger area of the gland, although containing only a few secondary nodules (Fig. 1). Often the dilated sinuses contained groups of lymphocytes, among which there were large cells with ingested chromatin granules in their cytoplasm, resembling the macrophages of reactive centers of lymph glands. The structure of the medulla, in the form of medullary cords, was not restored. However, clusters of plasma cells, sometimes very large, were seen in the bands of connective tissue close to the blood vessels.

Cells containing pigment, sometimes in large numbers, appeared at these times. Complete regeneration on the 20th day was found in 70% of grafts studied. Some grafts (30%) were replaced with connective tissue, initially by young granulation tissue later becoming transformed into scar tissue.

Series II—Grafts into Hybrids. When glands were grafted from the parent line into F_1 hybrids, massive cell destruction also took place in the first two days, after which regeneration began, differing somewhat from the regeneration after isografting.

On the 5th day the number of cells of "blast" type and of large lymphocytes increased in the lymphoid tissue regenerating at the periphery of the glands. Cells of the plasma series were found, many of them with degenerative changes: a few light vacuoles, thinning of the cytoplasm in some places, and often disintegrated and pycnotic nuclei. By the 20th day the grafts were clear of debris, but regeneration of their lymphoid tissue as a rule was incomplete. The central part of the glands remained free from lymphocytes and consisted of bands of reticular tissue (Fig. 2). The periphery of the gland was occupied by lymphoid tissue having the structure of the cortex of a lymph gland but without secondary nodules, usually in the shape of a semicircle or a complete ring. By one month or later the lymphoid tissue in some grafts had spread throughout the gland and become denser, so that the gland was becoming more and more like the isografts at the same times, but in other grafts regeneration was still incomplete even after 30-60 days. On the 20th day regeneration of the typical cortex was observed in 10% of grafts, and regeneration in the form of a semicircle of circle of lymphoid cells in 60%. As with the isografts, a few grafts were replaced by connective tissue.

Series III—Homografting. In the first two days after homografting of lymph glands from line A mice of lines $CBAT_6T_6$ and C56BL no significant differences were found from the picture of isografting and of grafting glands from mice of the parent line into hybrids. On the 2nd-5th day mitoses were sometimes observed in groups of lymphoid cells at the periphery of the gland, and the number of "blast" cells and large lymphocytes showed a slight increase. Conversely, considerably fewer small lymphocytes were seen than at the same times after isografting. A few groups of plasma cells could be seen at the peripher of the grafts.

The mass of debris had condensed and was gradually being absorbed. By the 8th day the number of lymphoid cells at the periphery began to decrease, and they had disappeared by the 12th-16th day. At these

times some grafts consisted of remnants of reticular syncytium surrounded by fibrous connective tissue, and scar tissue was found at this time in the place of others.

In the three variants of transplantation described, the grafted lymph glands were almost completely freed from their own lymphocytes in the first few days, and only small groups of lymphoid cells remained directly beneath the capsule. The reticular stroma was partially preserved. The stroma of the isografted gland was filled with lymphoid cells and the gland regenerated. Intact donor's lymphocytes evidently took part in the regeneration, as the ability of lymph glands to regenerate during explantation in organ cultures indicates [4]. Later, however, toward the 20th-30th day, the donor's lymphocytes were apparently replaced by the recipient's cells [6, 9, 10]. Some isografts (30%) die not regenerate, possibly as a result of disturbance of the normal circulation in the grafts.

No regeneration of lymphoid tissue took place in the homografts, and the glands were replaced by scar tissue.

When the glands of mice of the parent line were transplanted into hybrids the results differed slightly from those obtained during isografting. As a rule on the 20th day regeneration of the lymphoid tissue was retarded compared with that observed during isografting. This incomplete regeneration apparently depended on local conditions, possibly created by the activity of the donor's lymphocytes surviving in the transplanted gland and proliferating there. It may be supposed that they prevent repopulation by the "foreign" lymphocytes of the recipient.

Delay in repopulation by lymphocytes of the hybrid (recipient) may also be associated with deficiency of H-2 antigens of the second parent line in the stroma cells of the transplanted gland (donor). This would be a phenomenon allied to syngenic preference [7].

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