THE REGENERATION OF AUTOPLASTIC LYMPH NODE TRANSPLANTS.

By HENRY L. JAFFE, M.D., and MAURICE N. RICHTER, M.D.

(From the Laboratory Division of the Hospital for Joint Diseases and the Pathological Laboratory of Bellevue Hospital, New York.)

Plates 39 to 41.

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This work was undertaken as a companion study to that on transplantation of thymus previously reported (1). In spite of the extensive literature on tissue transplantation we found no references to the transplantation of lymph nodes. Since the results of these experiments were to be compared with those of thymus transplants in guinea pigs, we carried out the first experiment on this species. Our experiments were unsuccessful because the transplantation of cervical lymph nodes of stock guinea pigs invariably led to abscess formation, which, we believe, was due to the use of lymph nodes already infected. The necrotic tissue which results from transplantation is a favorable medium for the growth of bacteria present in the nodes. Even the use of young guinea pigs, about 25 days of age, frequently gave the same result. We abandoned the experiments on guinea pigs, and used albino rats, which are quite resistant to pyogenic infection. We used rats between 3 and 5 weeks of age, and transplanted cervical nodes which were normal in gross appearance. Successful transplants were obtained in over 90 per cent of the cases. Whole lymph nodes were planted in pockets of the abdominal wall, by the same technique that was used in the transplantation of thymus.

In all, 31 albino rats were used, in each of which two nodes were transplanted simultaneously. In this series of 62 transplantations there were but four instances of infection.

The transplants were studied at about 24 hour intervals from the 1st to the 12th days, and at longer intervals up to 35 days. Most of the plants were removed between the 2nd and 7th days, as this is the period of most active regeneration.

The tissues were fixed in Bouin's fluid, Helly's fluid, or alcohol. The Bouin- and some of the Helly-fixed tissues were embedded in paraffin and stained with hematoxylin and eosin, Van Gieson, iron-hematoxylin, or phosphotungstic acid-hematoxylin. The plants fixed in alcohol were stained with pyronine and methyl green. Some of the Helly-fixed nodes were sectioned in celloidin, and stained with azure B-methylene blue-eosin (2). This last method gave the best preparations for studying the details of regeneration.

OBSERVATIONS.

Minor differences were observed in transplants of the same age even in the same animal. The following account is an approximation of the changes observed with reference to the time after transplantation.

At the end of 24 hours, there is extensive necrosis in the center of the transplant involving mainly the lymphocytes. At the periphery of the node some normal appearing lymphocytes are seen. Surrounding the node is a space, probably the peripheral lymph sinus of the transplanted node, which in some areas contains a few lymphocytes. Most of the reticulum of the transplant is preserved, though obscured in the central portions by the cellular debris. The vessels in the tissue around the transplant are not dilated, and the only reaction to the transplant is a slight polymorphonuclear infiltration between the muscle fibers about the transplant.

By the end of the 2nd day, three well defined areas are visible in the transplant: a central necrotic area, a peripheral margin of well preserved tissue, and an intermediate zone of hyperplastic reticulum (Figs. 1 and 2). Considerable liquefaction and absorption have taken place, so that the necrotic area is reduced in size. The reticulum contains numerous mitotic figures. The marginal zone contains mainly small lymphocytes and an occasional large lymphocyte. Mitotic figures in the lymphocytes are difficult to find. At the hilus of the node dilated vessels filled with blood penetrate the transplant, and their subdivisions extend to the periphery. The cellular reaction about the transplant is not extensive.

During the 3rd day, the necrotic mass becomes smaller, and the reticulum becomes more prominent. Large phagocytic cells in the reticulum aid in the removal of the debris. At the margin is a zone of small lymphocytes, among which are a few large lymphoid cells. Large lymphoid cells are formed from the reticulum in areas where reticulum cell hyperplasia is most prominent, and are therefore formed extravascularly. The formation of lymphocytes from tissue cells is also observed in the connective tissue outside the transplanted node.

During the 4th day, the debris is almost completely removed. The transplant now appears more like a normal lymph node, with very vascular connective tissue at the hilus (Fig. 3). Extravascular formation of lymphocytes from tissue cells is observed in areas both in and outside of the node. The peripheral lymphocytic

zone is wider. There are no germinal centers, but scattered small groups of large lymphoid cells, identical with germinal center cells, are observed. There is a tendency for the lymphocytes to be arranged in cords, extending from the periphery to the medullary portion.

After 5 days, regeneration is nearly complete. The transplant now appears as a normal lymph node. The lymph capillaries at the hilus are filled with lymphocytes and are efferent vessels (Fig. 4). The reticulum is still prominent, and mitoses may be observed. Large lymphocytes are scattered among the smaller cells of both the cortex and medulla.

At 6 days the node is completely regenerated. The efferent capillary lymph vessels previously observed may be traced from the hilus into the surrounding tissue.

At periods from 6 to 35 days, sections show that the transplant persists as a fully developed lymph node in the muscles of the abdominal wall. No retrograde changes were noted (Figs. 5 and 6).

DISCUSSION AND SUMMARY.

The reticulum plays an important part in the regeneration of lymph nodes autoplastically transplanted into the abdominal wall of the albino rat. The necrosis which follows transplantation involves mainly the lymphocytes. A margin of lymphocytes is preserved only at the periphery. This may be due to early lymphatic connection with the marginal sinus of the node. The reticulum cells are apparently more resistant since for the most part they do not degenerate. There are three possible origins of the lymphocytes of the regenerated node. They may arise by proliferation of lymphocytes retained at the periphery of the plant. The presence of a few mitotic figures among lymphocytes in the marginal region confirms the possibility of this mode of origin. They may also be derived from lymphocytes brought into the transplant by the blood or lymph circulation. Though some lymphocytes are present in the marginal sinus, and an occasional lymphocyte is seen in the capillaries which enter at the hilus, we believe that this source of origin of the lymphocytes is negligible. On the other hand, the hyperplastic reticulum appears to be the important source of lymphocyte production. These may be derived from the reticulum directly as small lymphocytes, or may be formed through the intermediary stage of large lymphoid cells. This capacity is not limited to lymphatic reticulum, as small foci of lymphocyte formation are found in the connective tissue in the vicinity

of the transplants. The reticular origin of lymphocytes is most easily observed in the earlier stages of regeneration before the picture is obscured by the numerous small lymphocytes.

Two structures in the regenerating node are directly traceable to the same structures of the transplant. These are the marginal sinus and the hilus. The marginal sinus of the transplant is preserved, and is probably an important means by which lymphatic communication is established with the surrounding tissue. The hilus is the site of entry of the blood vessels, and the hilus of the regenerated node is the same as that of the transplant.

BIBLIOGRAPHY.

1. Jaffe, H. L., Autoplastic thymus transplants. II. With particular reference to the regeneration of the reticulum cells and the formation of Hassall's corpuscles, *J. Exp. Med.*, 1926, xliv, 523.
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EXPLANATION OF PLATES.

PLATE 39.

FIG. 1. 2 days. Shows three well defined areas. Central necrotic zone, zone of well preserved lymphocytes, and intermediate zone of hyperplastic reticulum. Hematoxylin and eosin. ×37.

FIG. 2. Higher magnification of the three zones shown in Fig. 1. Hematoxylin and eosin. ×112.

PLATE 40.

FIG. 3. 3 days, 17 hours. The cellular debris has practically disappeared and its place is taken by a vascular reticulum with many newly formed capillaries. There is a peripheral zone of normal appearing lymphocytes. Eosin-azure B-methylene blue. ×72.

FIG. 4. 5 days. Almost complete regeneration, but with prominent reticulum in the center. Efferent lymph channels contain many lymphocytes. Hematoxylin and eosin. ×55.

PLATE 41.

FIG. 5. 7 days. Complete regeneration of transplant. Hematoxylin and eosin. ×32.

FIG. 6. 21 days. Regenerated lymph node transplant after 21 days. No retrograde changes. Hematoxylin and eosin. ×37.

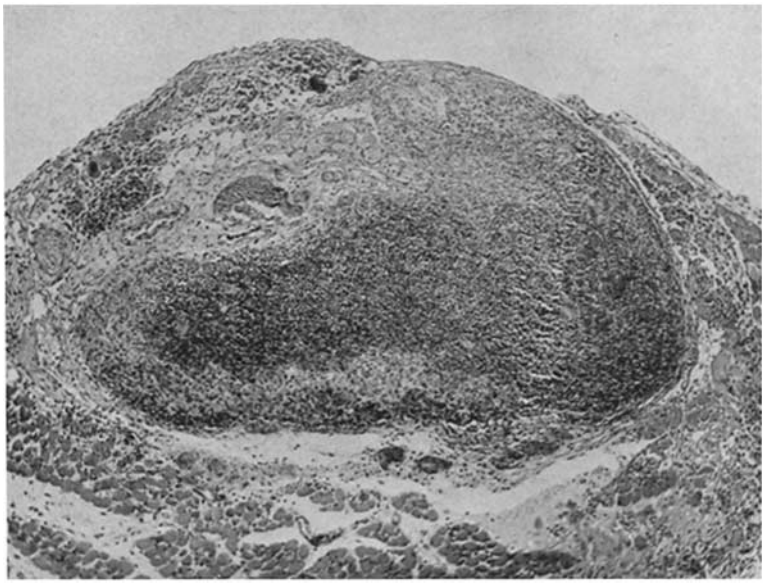

FIG. 1.

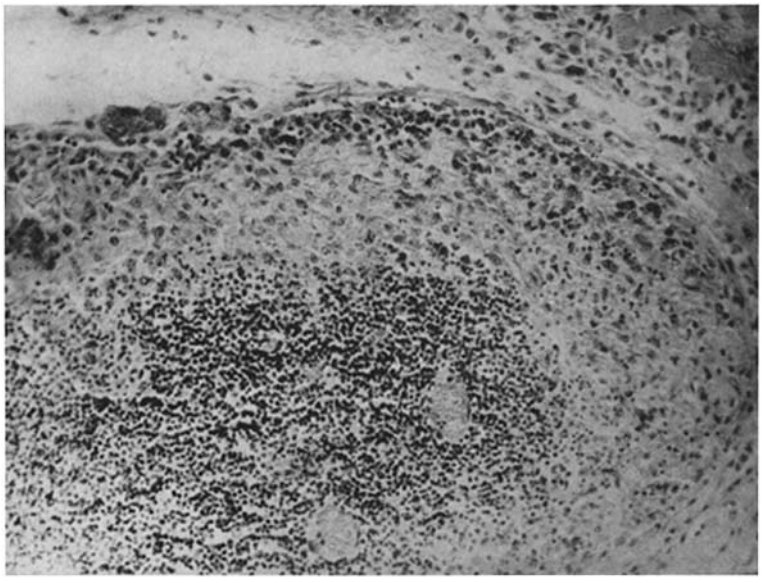

FIG. 2.

(Jaffe and Richter: Autoplastic lymph node transplants.)

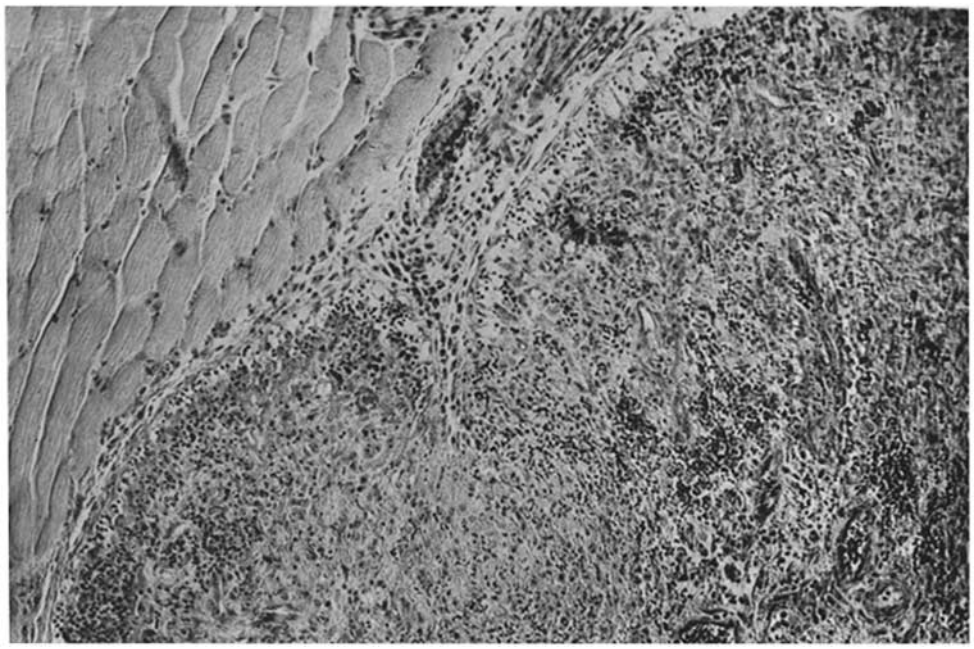

FIG. 3.

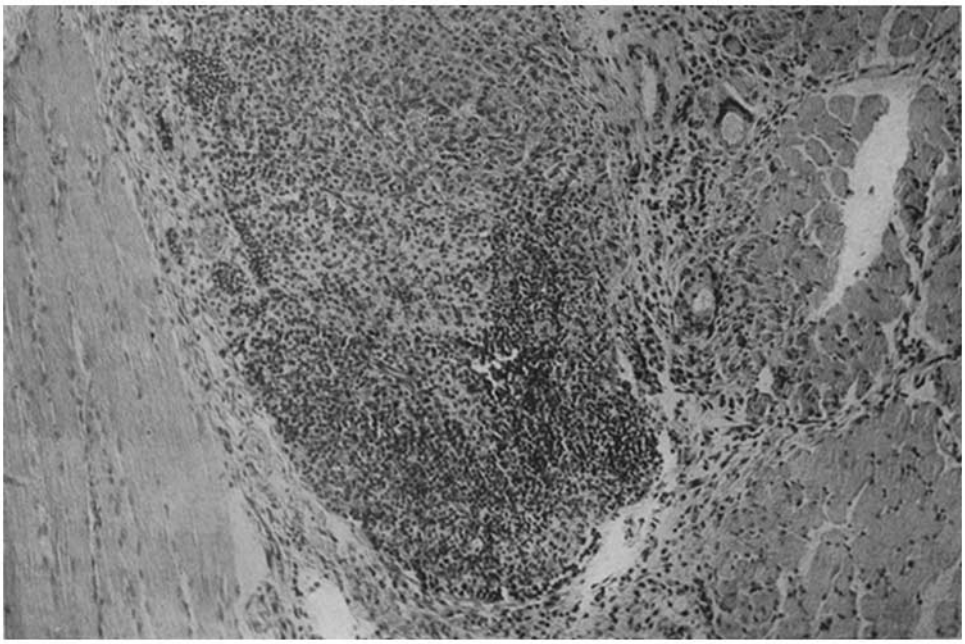

FIG. 4.

(Jaffe and Richter: Autoplastic lymph node transplants.)

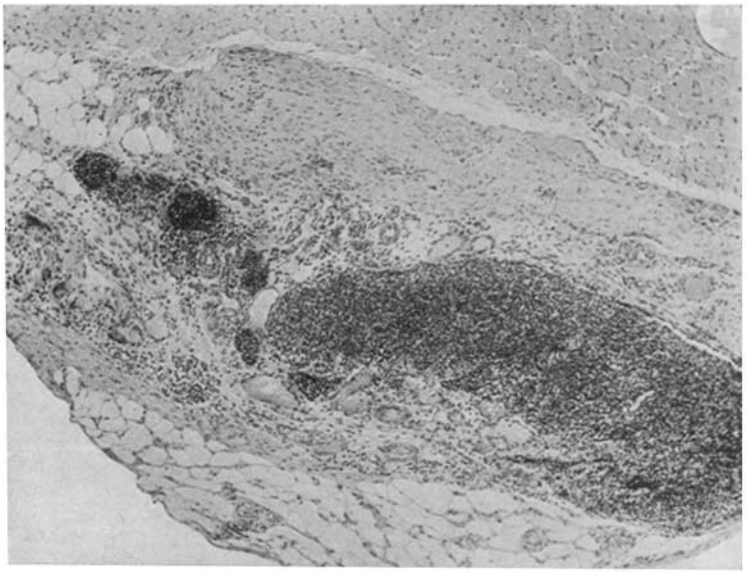

FIG. 5.

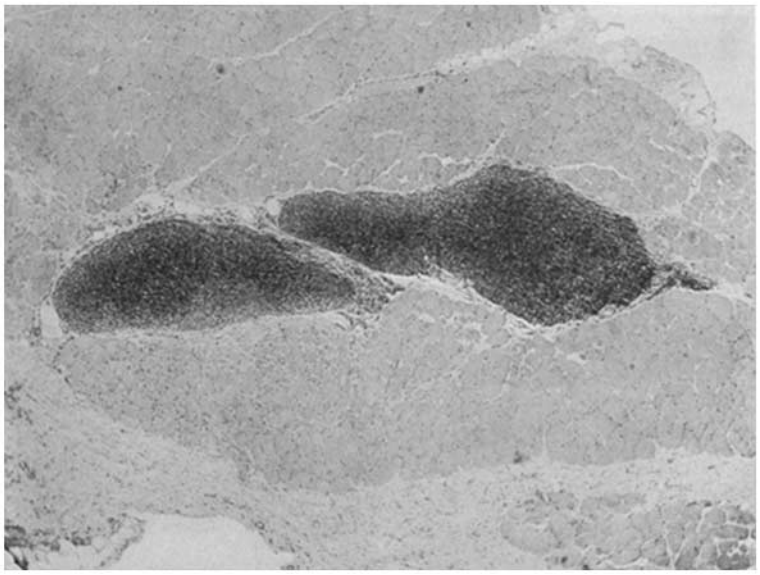

FIG. 6.

(Jaffe and Richter: Autoplastic lymph node transplants.)