Regeneration and Autotransplantation of Lymph Nodes *

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PREVIOUS STUDIES demonstrated the rapid regeneration of lymphatics and the early restoration of lymphatic circulation that follows transection of a limb.[2] Subsequently it has been demonstrated that a lymph node can survive if its vascular pedicle is severed, the viability being dependent upon the flow of lymph. Also, if only the lymphatics to a lymph node are severed, the node not only survives but the lymphatics regenerate, restoring the lymph circulation through the nodes.[4]

* Submitted for publication April 23, 1964.

Supported by Grants CA 05622 and HE 04182 from the National Cancer and Heart Institutes, USPHS and from the American Heart Association.

The purpose of this study was to investigate the regeneration of lymphatics when 1) a lymph node is excised, 2) the medulla is enucleated from the lymph node or 3) the lymph node is transplanted as a free autograft to a different part of the body.

Methods

The investigation concerned the popliteal lymph nodes in mongrel dogs. Preoperative lymphangiograms of the hind limbs were performed using Hypaque (50%) as the contrast medium. The Hypaque was mixed with hyaluronidase and injected subcutaneously. Lymphangiograms were taken im-

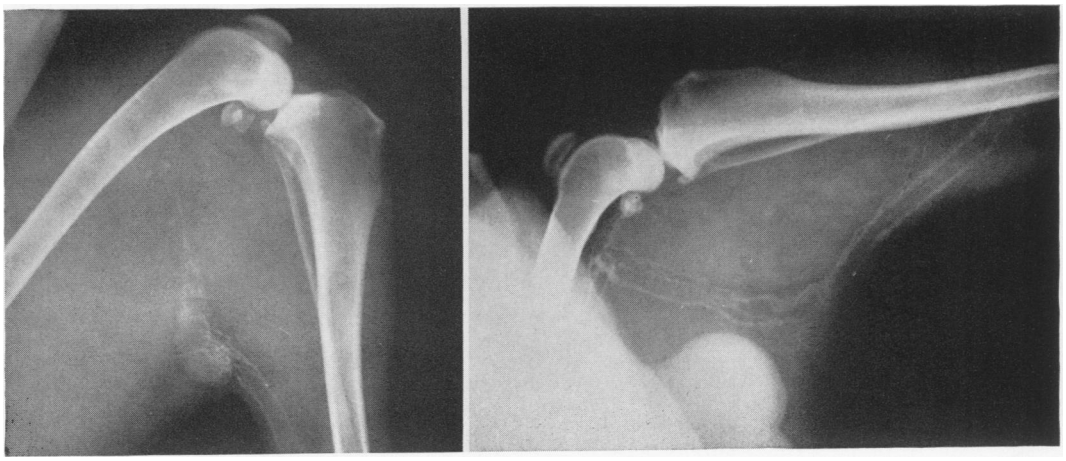

FIG. 1 A. Control lymphangiogram before excision of the popliteal lymph node.
B. Lymphangiogram 145 days after excision of popliteal lymph node. Note absence of regeneration of lymphatic vessels.

FIG. 2 A. Preoperative lymphangiogram before enucleation of medulla from within capsule of node.

B. 25 days after resection of medulla from capsule. Continuity of lymph flow has been restored.

C. 125 days after resection of medulla, lymphangiography suggests regeneration of node.

mediately, utilizing methods previously described.[1]

Following preoperative lymphangiography, these operations were performed in respective series:

1. The popliteal lymph node was excised, all lymphatics to and from the node being ligated (5 dogs). The wound was closed primarily.

2. The popliteal lymph node was incised over its external surface and its medulla was enucleated (8 dogs). It was easy to shell out the medulla from the capsule as a definite plane of cleavage exists. The blood vessels to the node were divided (intracapsularly) between ligatures, *preserving intact the afferent and efferent lymphatics.* The capsule of the node was then closed with catgut and the soft tissues were closed primarily.

3. The medulla of the popliteal lymph node was enucleated (7 dogs), as described above, after which the medulla from the contralateral popliteal lymph node was sliced in thin sections and inserted into the capsule of the ipsilateral node as an intracapsular autograft. The capsule and wound were then closed primarily.

4. The entire lymph node was excised (4 dogs), sliced in thin slices and inserted as free autografts in the popliteal fossa of the opposite side. Before the graft was inserted the recipient bed was prepared by excision of the respective node, all lymphatics to the excised node being ligated.

In each series lymphangiograms were performed every week during the first month after operation, every 2 weeks during the second month and then monthly for a total follow-up period of 5 months. After 5 months the popliteal lymph nodes were excised for histologic examination.

Results

Complete Excision of Lymph Nodes. Following excision of a lymph node the

wounds healed primarily and lymphedema distal to the node was not detected. Within a day or two after the node was excised, lymphangiography demonstrated the afferent lymphatics to be obstructed (ligated) at the popliteal fossa. Repetition of the study after another few days showed pooling of "lymph" in the wound. After a period of about 3 weeks, regeneration of the lymphatics across the popliteal fossa was radiographically visible (Fig. 1 A). In no instance did a lymph node reform but regeneration of the lymphatic vessels was so perfect that at the time of sacrifice (after 145 days), lymphangiography often failed to give any indication that a lymph node had ever been present in the popliteal fossa (Fig. 1 B).

Enucleation of Medulla of Lymph Node. As mentioned above, enucleation of the medulla was an easy procedure, leaving a well formed fibrous capsule without any gross evidence of residual medulla. In these instances the lymphatics were not ligated but the capsule of the lymph node was closed, thereby providing a mechanism for the pooling of lymph within the capsule. Radiographically this pooling of lymph was quite evident, but channels became organized after about 2 weeks. After approximately 4 weeks, lymphangiography suggested the regeneration of the lymph node itself. In all but two instances radiographic evidence of regeneration became marked although the architectural pattern remained abnormal (Fig. 2 A, B, C). Histo-

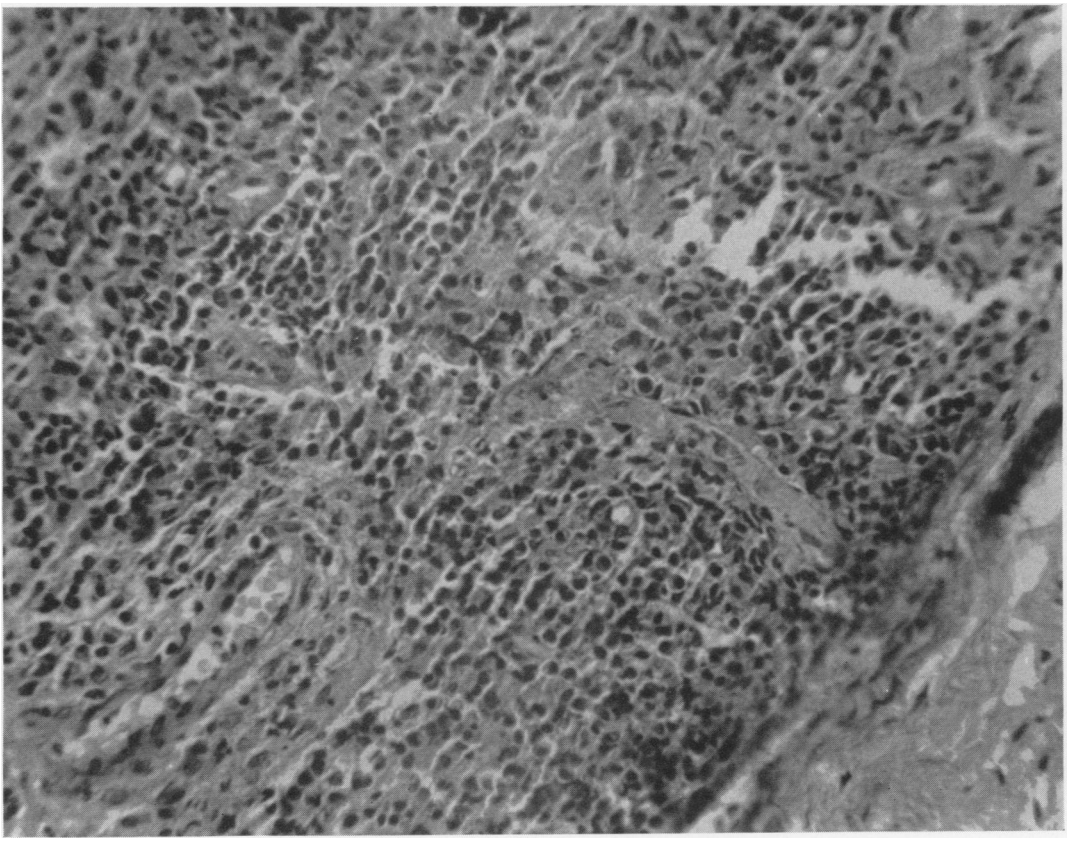

FIG. 2 D. Photomicrograph of lymph node 155 days after resection of medulla from capsule. Regeneration of node has occurred.

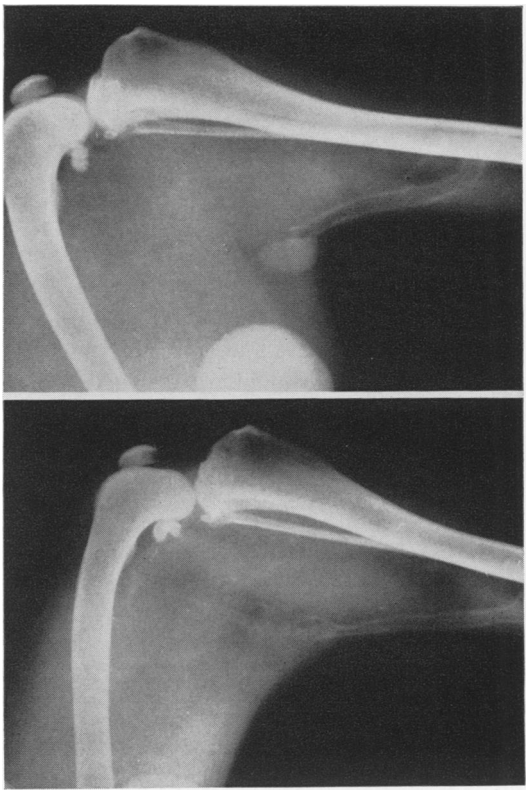

FIG. 3 A. Preoperative lymphangiogram before grafting of medulla from opposite node.

B. 28 days after grafting the contralateral medulla into the ipsilateral capsule. Restoration of flow has occurred but no lymph node is visible.

logically the excised lymph node revealed distinct evidence of viable lymphoid tissue in four instances (Fig. 2 D). Actively proliferating germinal centers with fibrous septa had regenerated.

Grafting of Medulla to the Capsule of the Opposite Leg. Following grafting of the medulla the sequence of events radiographically appeared to be somewhat similar to those in which the medulla was enucleated but not grafted. The lymph node showed radiographic evidence of reorganization with the restoration of lymph flow through the capsule (Fig. 3 A, B). After 160 days, the "node," when present, appeared radiographically to be small and abnormal in its architectural pattern. In two instances nothing resembling a residual lymph node could be found and in only one instance did the nodule, radiographically resembling a lymph node, contain lymphoid tissue when studied histologically (Fig. 3 C).

Grafting of Sliced Lymph Nodes. Following grafting of the entire sliced node, the sequence of events radiographically was as described above with initial pooling of lymph followed by reorganization and restoration of the lymph flow across the popliteal wound (Fig. 4 A, B, C). Lymphangiograms sometimes suggested the presence of a "node" in the popliteal area. In two instances a small fibrotic nodule was found at the time of re-exploration of the wound. The nodules were so hard, however, that they could not be cut; histologic evidence of successful grafting was never obtained.

Discussion

The lymphatic system has a remarkable property of survival and regeneration. As was shown earlier a lymph node can survive, and apparently function normally, after division of its blood supply or its lymphatic connections.

The lymph node does not reform after complete excision. In the five experiments in which the popliteal lymph node was completely excised there was no evidence of regeneration of any node. Although the lymphatics were ligated with fine silk before they were divided, the contrast medium later was found to extravasate, collecting in the popliteal wound for several days after the operation. Necrosis of a thin-walled, delicate lymphatic vessel after ligation is not surprising. Lymphedema did not develop as lymphatic drainage from the foot apparently remained adequate due to the competence of collateral pathways. Regeneration of the lymphatics across the wound,

from which the node had been excised, was anatomically remarkable.

Following removal of the medulla from within the capsule, new lymphoid tissue formed in at least four instances. Enucleation of the medulla from the capsule appeared initially to have been complete. Possibly a bit of medulla was overlooked and provided the focus for regeneration. Another possibility is that the capsule, bathed by the lymph stream, has the power to collect lymphopoietic cells and to form new lymphoid tissue.

Grafting the medulla did not appear promising. It was hoped that the capsule would provide a pool or stream of lymph which might maintain the viability of the intracapsular graft. The follow-up studies indicated that although the lymphograms suggested viable lymph nodes (successful grafts), histologically these nodules were fibrotic, contracted capsules with channels through which lymph flowed. Regeneration of lymphoid tissue occurred *without* the graft; with the graft lymphoid tissue was seldom demonstrable. Perhaps necrosis of the graft produced a deleterious effect.

The fact that lymphoid tissue can remain viable under relatively adverse conditions yet might permit successful autografting of lymphoid tissue. Nanson [8] indicated that if the whole node (i.e., with its capsule) is grafted to another site it sometimes survives. Maintenance of a blood

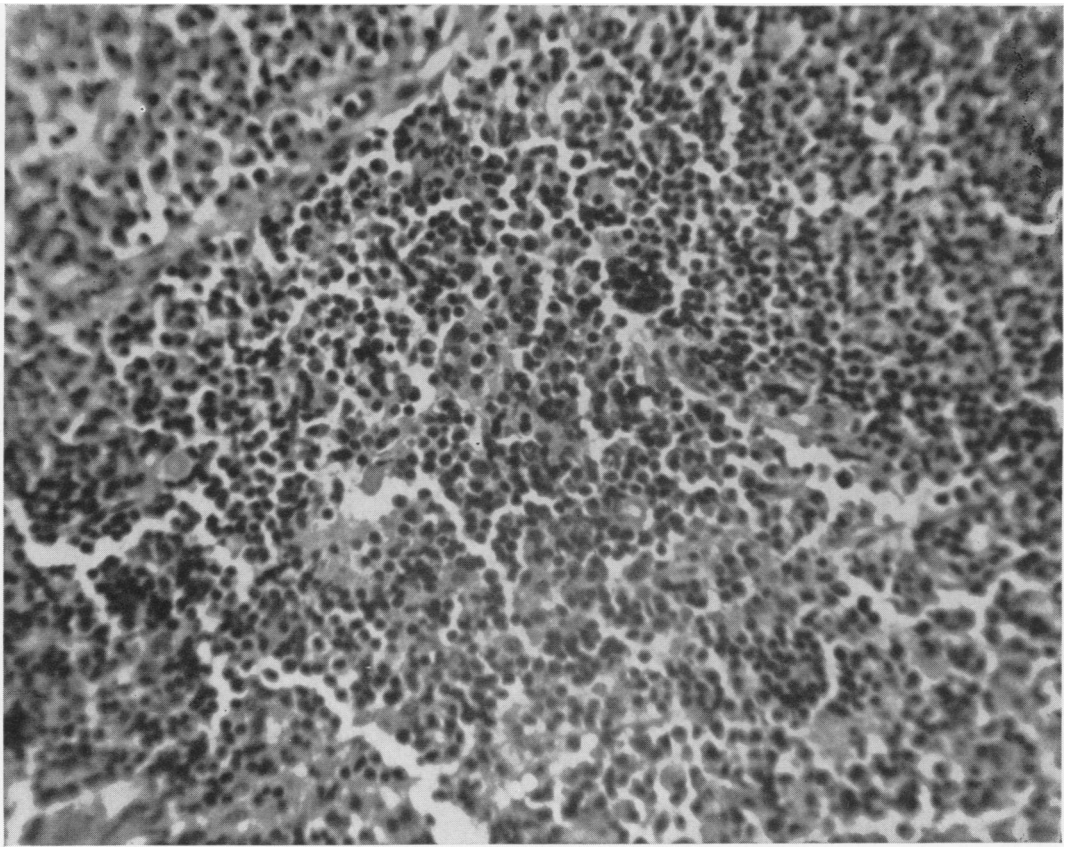

FIG. 3 C. Photomicrograph of one lymph node 160 days after grafting opposite medulla in original capsule. This probably represents regeneration rather than a successful graft.

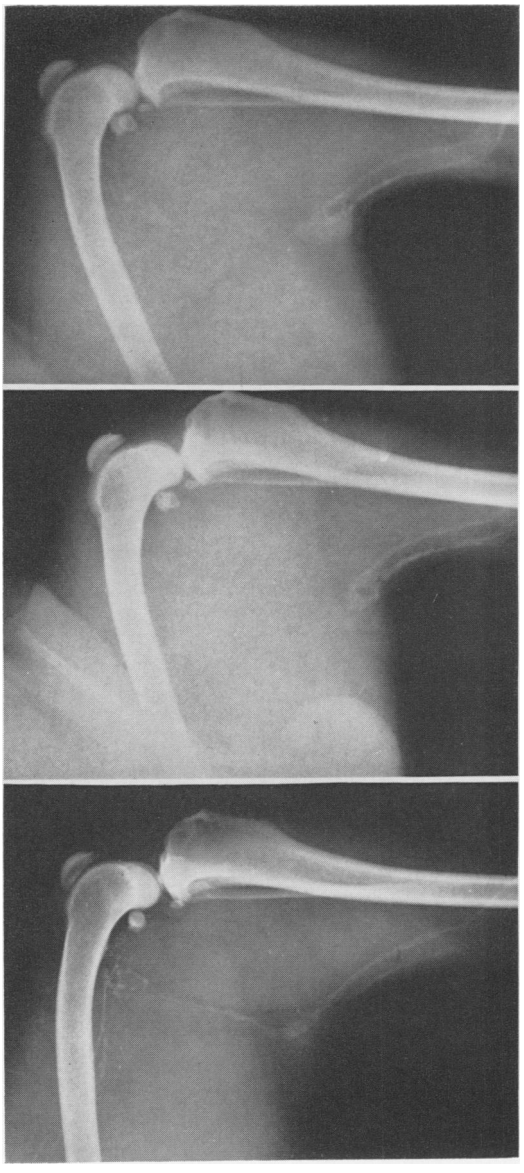

FIG. 4 A. Preoperative lymphangiogram prior to autografting sliced node.

B. 17 days after grafting sliced lymph node, reorganization is occurring.

C. 61 days after grafting sliced lymph node. Histologically no lymphoid tissue was found in grafted node.

supply to an autografted node should certainly permit its viability. That such a grafted node would reform connections with afferent and efferent lymphatics remains to be demonstrated. If technically and biologically feasible, such autografts could be useful after exterpative operations for cancer or in the treatment of congenital or acquired lymphedema.

Summary

Excision of a single lymph node in the dog is followed by rapid restoration of the flow of lymph across the wound as new lymphatic channels develop to restore continuity. The lymph node does not regenerate.

Excision of the medulla of a lymph node with closure of the capsule of the node is followed by rapid healing and maintenance of flow through the capsule. Lymphangiographically and histologically, regeneration of the node sometimes ensues. Slices of the entire lymph node or of its medulla failed to survive as free autografts.

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