

Regeneration of Lymphatic Vessels: *

A Radiographic Study

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WITH the development of lymphangiography by the simple technic of subcutaneous injection of the radiopaque medium, serial studies of lymphatic regeneration in the dog became practical. Lymphatic endothelium, like capillary endothelium, has remarkable powers of regeneration. Investigators have studied regeneration of the lymphatics in healing wounds by several methods. In earlier studies, lymphatics were visualized by means of subcutaneous injections of either Evans Blue or India Ink dyes. Surgical exposure of regenerated lymphatics was required in such investigations in order to identify the vessels.^{1, 2, 4-6, 9-11}

Following complete section of the lymphatics of a limb, the resulting edema is of short duration, subsiding as lymphatics regenerate.⁷ On the other hand, no regeneration has been found after resection and ligation of short segments of a large lymphatic trunk.¹⁰ The present study consists of two different experiments, each performed on a respective group of ten dogs.

Regeneration Following Transection of Lymphatics

In this group, the operation described by Halsted and Reichert^{7, 11} was carried out (Fig. 1). The tissues of the posterior

thigh at the middle third, with the exception of the femur, femoral artery and vein and femoral and sciatic nerves, were completely transected. Following transection, the wound was closed primarily. At the time of operation, the lymphatic vessels were visualized by means of injection of Evans Blue dye into the paw in an effort to insure that none of the perivascular or perineural vessels would escape transection. This additional precaution seemed necessary since the number of lymphatic trunks along the femoral vein is variable and consequently it is possible to overlook one unless colorimetric visualization is achieved.

In the postoperative course, each dog developed marked edema of the limb, distal to the transection. Edema started on the first postoperative day and increased in the following days. By the fourth or fifth day it reached its peak; after which it started to subside. *By the end of the third week, edema was completely gone and function of the leg was completely reintegrated.* Two of these dogs developed a discrete wound infection with dehiscence of 5.0 and 7.0 cm., respectively. In these two dogs, edema persisted a few days longer than it had in the others, but by the end of a month it had completely subsided.

Radiographic studies consisted of a preoperative lymphangiogram (Fig. 2) and a follow up lymphangiogram every two weeks during the first month following

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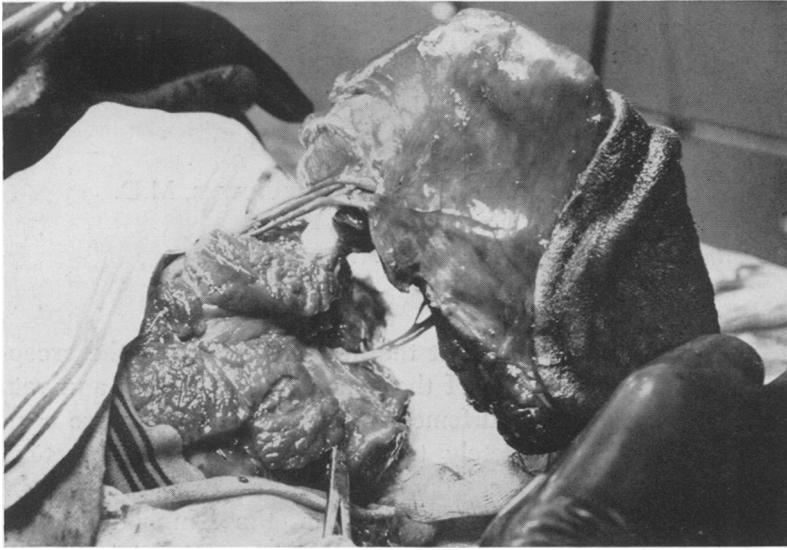


FIG. 1. All soft tissues were severed in the middle third of the thigh except for the femoral artery, vein and nerve, the bone and the sciatic nerve.

operation and thereafter, monthly, for six additional months.

The first *postoperative* (two weeks) radiogram failed to outline any lymphatic vessel cranial to the line of transection. Instead there was noted uniform opacification of the soft tissues peripheral to the wound as if the contrast medium were present throughout these tissues. Discrete lymphatics could not be identified.



FIG. 2. Preoperative normal lymphangiogram of a dog of the first (transection) group.

Lymphangiogram taken four weeks *postoperatively* (Fig. 3) showed a rich network of lymphatic vessels traversing the line of transection. There was, in fact, a greater number of vessels demonstrated at

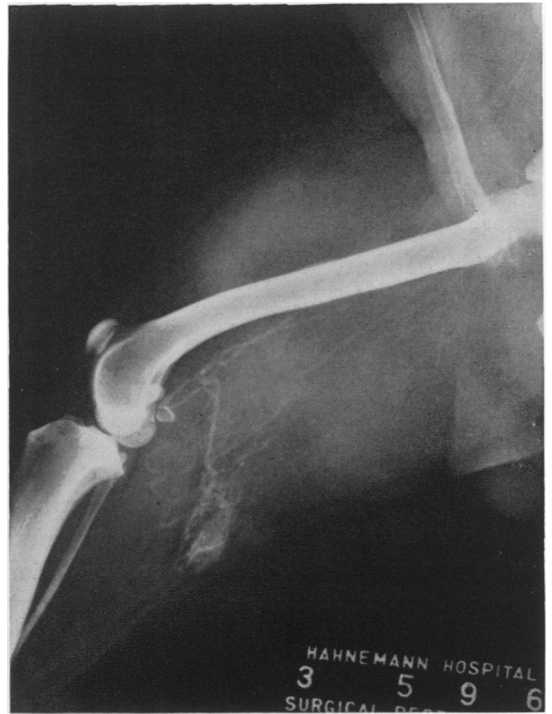


FIG. 3. Four weeks after transection, a rich network of collateral lymphatics is evident.



FIG. 4. Eight weeks after transection, the preoperative pattern is restored.

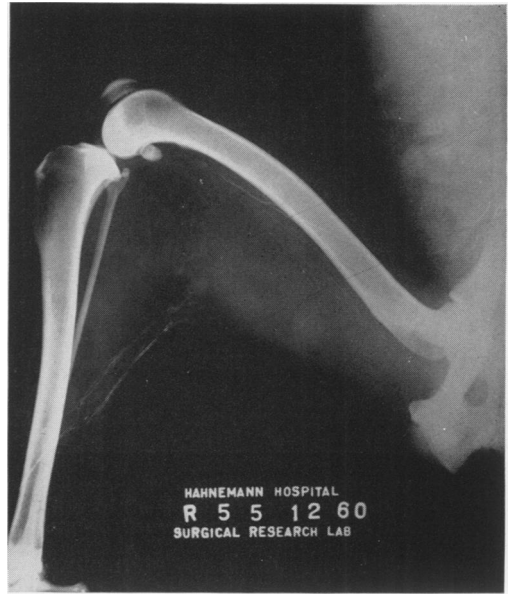


FIG. 5. Preoperative normal lymphangiogram of a dog of the second (resection) group.

this stage than in the normal preoperative film.

By the end of two months large lymphatic vessels, similar to the original ones, were visualized, while many of the small

communicating vessels previously seen no longer filled (Fig. 4). Subsequent lymphangiograms demonstrated no further changes. The normal pattern had essentially been restored.

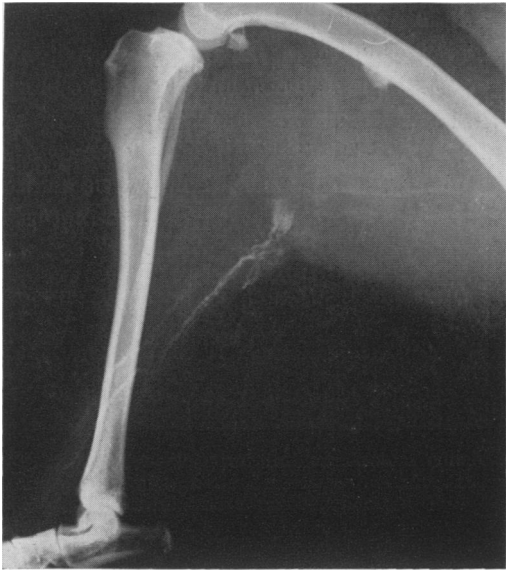


FIG. 6. Six weeks after the resection a collateral group of lymphatic vessels is evident; the resected main trunks have not regenerated.

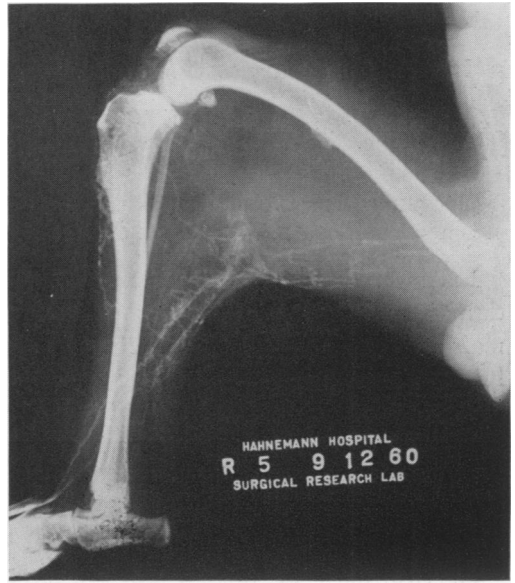


FIG. 7. Three months after the resection; this group of collateral has become enlarged and tortuous.

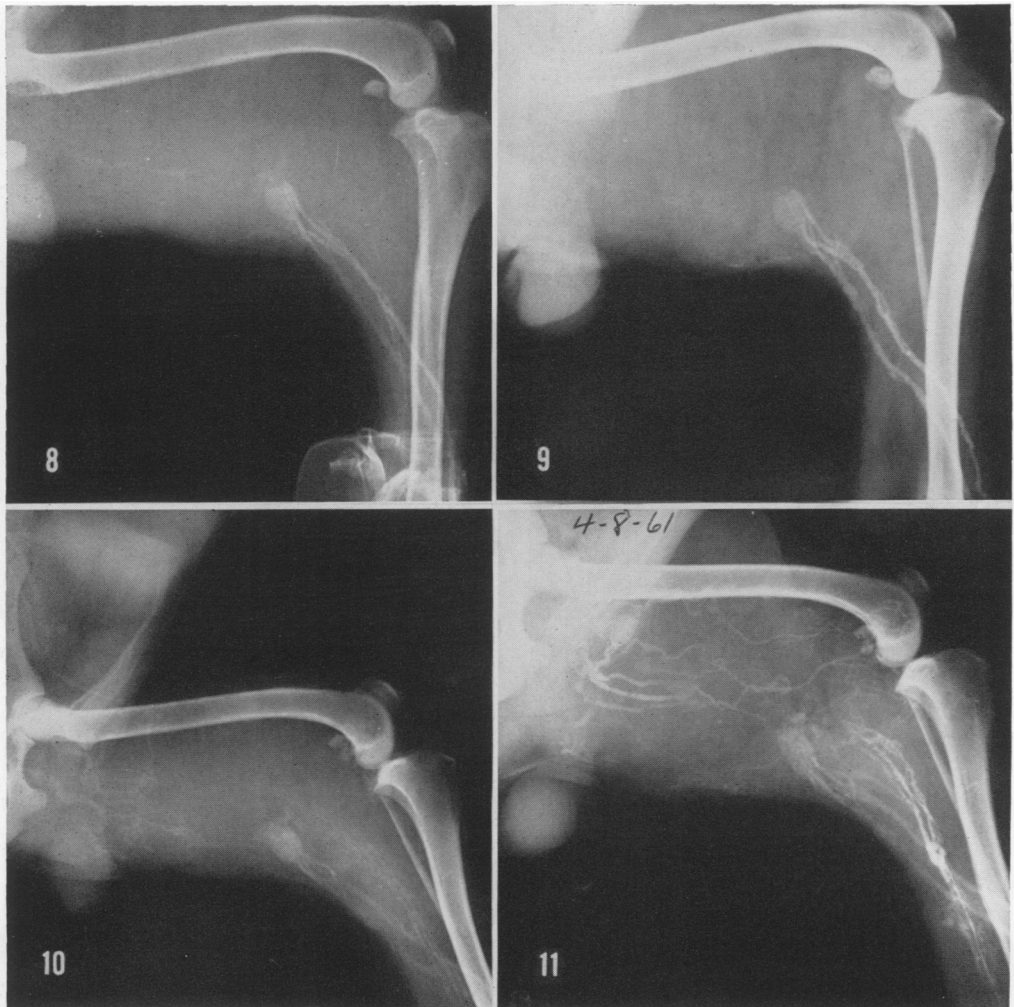


FIG. 8, 9, 10, 11. Follow up (1 year) of another dog after resection shows progressive dilatation of the lymphatic vessels.

Regeneration Following Resection of Lymphatics

In these dogs complete transection as described for the preceding group of animals was performed. In addition, main lymphatic trunks running along the femoral vein, identified by Evans Blue dye, were carefully and completely *excised from the inguinal crease to the popliteal lymph-node*. This node was also partially resected. The wounds were closed primarily.

In two dogs of this group the post-operative course was complicated by infection and dehiscence of the wound, 8.0

and 10 cm. in length. These wounds appeared completely healed by the end of the fifth week.

In eight dogs with no complication of wound healing, the edema subsequent to the procedure disappeared between the third and fourth weeks. Two of these dogs were observed for a period of one year. During the second six months, one animal demonstrated recurrent swelling of the leg of moderate degree.

The first radiographic follow up on this group was also performed after two weeks; no lymphatics cranial to the line of transec-

tion were visualized. The radiogram taken after six weeks showed groups of lymphatic vessels on the medial aspect of the thigh (Fig. 5, 6). By three months the lymphatics were becoming dilated and tortuous (Fig. 7). Subsequent x-ray studies failed to demonstrate any regeneration of the resected main lymphatic vessels. The collateral vessels became progressively enlarged, tortuous and more numerous in the two dogs which were observed for one year, as demonstrated radiographically (Fig. 8, 9, 10, 11). In all but three of the dogs the partially resected lymphnode remained *functional*, being subsequently visualized in continuity with lymphatics on the medial aspect of the thigh.

As mentioned above, in two dogs the postoperative course was complicated by infection and dehiscence of the wound. In these two dogs, edema at the end of the fourth week was still marked. By the end of the second month it was less conspicuous, but after that remained stationary. One of these dogs died three months after the procedure with edema of the involved

leg; the other dog still has edema of the leg after 13 months.

In these latter two dogs, radiographic follow up demonstrated, at four weeks, inadequate formation of lymphatic vessels at the line of transection as well as beyond it. The lymphatic vessels of the leg remained appreciably larger than demonstrated on the preoperative film. In subsequent lymphangiograms lymphatic vessels were seen to remain dilated with slight restriction across the line of transection (Fig. 13). This abnormality has partially regressed, but in the dog surviving for 13 months enlargement of the lymph vessels is still conspicuous (Fig. 14).

Discussion

Performance of lymphangiography by the indirect technic has made possible a more detailed long-term study of lymphatic regeneration following division or excision. Failure to visualize regenerating lymphatics earlier than two weeks probably is a limitation of the technic used, because Reichert, using direct exposure and local

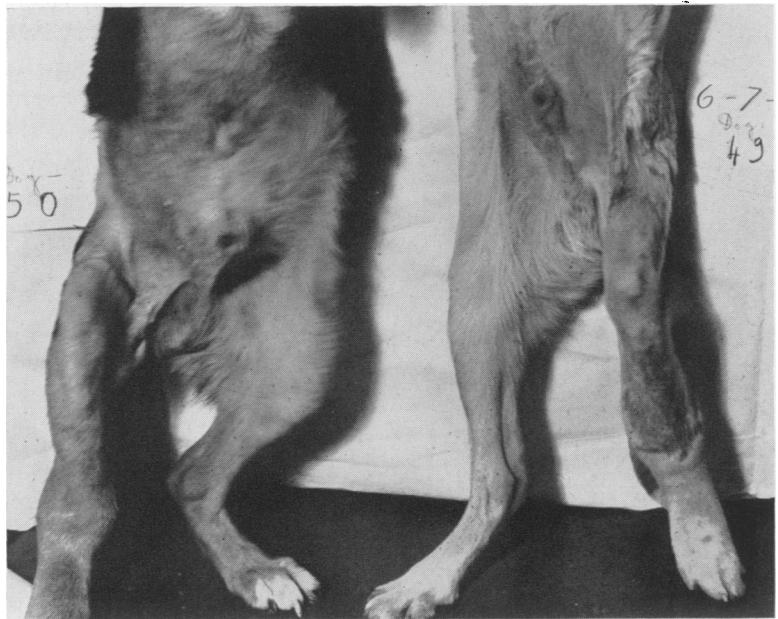


FIG. 12. In the two dogs of the second group which developed infection of the operative wound, the postoperative edema of the leg never regressed; photograph of these dogs three months after the procedure.

injection of dye, demonstrated that regeneration of the lymphatic capillaries begins a few days after section. The same investigator has shown that a longer period of time is required for regeneration of larger vessels.¹¹

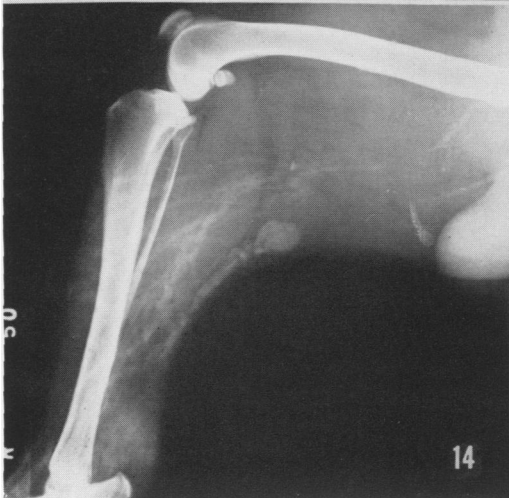


FIG. 13, 14. Lymphangiograms of one of two dogs with wound infections three months and one year,¹² respectively, after the procedure; the lymphedema of the legs persists without appreciable modification.

After surgical *transection* of lymphatics, edema appears peripheral to the site of division. Within a few days, lymphatic capillaries regenerate, followed in two to three weeks by regeneration of larger trunks. During the period of edema, normal drainage via larger lymphatic trunks is interrupted and lymphatics peripheral to the wound are dilated. Once drainage is re-established by regeneration of lymphatic trunks, edema disappears and peripheral lymphatics gradually return to their original size. Infection in the surgical wound retards or permanently distorts resumption of normal lymphatic drainage. The final radiographic configuration after *transection* of lymphatics can hardly be distinguished from the one preceding the operation. Long-term follow up studies demonstrate that the normally restored pattern does not subsequently regress.

In the group of dogs which underwent *resection* of the main trunks, dilated collateral vessels also appeared. Since resected trunks did not regenerate, the collateral group did not regress. Instead they became large and tortuous. They served, however, to effect functionally adequate drainage of the limb for at least several months. The location of this collateral group has been demonstrated by surgical dissection to be on the medial aspect of the thigh, either subcutaneously or in proximity to the sciatic nerve. This fact suggests that this group, rather than being newly formed, results perhaps from the dilatation of pre-existing small vessels which under normal conditions are not evident on the lymphangiogram. In two animals observed for more than a year these collateral vessels became progressively more dilated and tortuous as shown by lymphangiography. After eight months mild edema reappeared and persisted, possibly on the basis of valvular incompetence in the dilated lymphatics.

The observation that local infection in

the operative field interferes with normal lymphatic regeneration and re-establishment of lymphatic drainage is in agreement with previous work by others.⁸ It is interesting to note that in this study, stripping of the main lymphatic trunks complicated by severe infection produced a lasting lymphoedematous state which in one dog is already more than one year in duration.

Conclusions

Transected lymphatic vessels regenerate, regaining their anatomical continuity and function. Those lymphatic vessels visualized by lymphangiography, e.g. the main trunks, are restored to a near normal configuration within one month. Since edema begins subsiding earlier, it appears that lymphatic drainage in an intermediate period is mainly through capillary vessels which cannot be visualized by lymphangiography.

Segments of main trunks which are *resected* do not regenerate. The lymphatic drainage is re-established rather efficiently by a collateral group. Secondary insufficiency of this group with consequent late reappearance of edema has been observed, possibly due to valvular insufficiency. Infection of the operative wound exerts a deleterious effect on the regeneration of lymphatics and may, under specific conditions, lead to chronic lymphoedema.

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