

ANNALS OF SURGERY

Vol. 139

FEBRUARY, 1954

No. 2



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THE LYMPHATIC CIRCULATION IN LYMPHEDEMA*

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FIFTEEN PATIENTS with idiopathic lymphoedema of the lower limbs have been studied while undergoing treatment. Twelve were typical cases of lymphoedema praecox of spontaneous onset during the second or third decades of life. One was a case of true congenital familial lymphoedema. Another had, together with the typical features of lymphoedema, changes in the blood vascular system of the limb in the form of cutaneous naevi and overgrowth of the bones constituting a giant limb of the type described by Robertson.¹¹ A third case had blood plasma proteins of a lower level than normal. These three cases with additional less typical features have been included because of the findings in the studies of their lymphatic anatomy and circulation were similar to those in the rest of the series.

No cases of lymphatic edema due to obstruction by malignant disease have been included, although findings from some are referred to for comparison.

METHODS OF STUDY

Each patient was fully examined by the usual physical methods. Constitutional causes of edema such as cardiac or renal factors were excluded. Phlebographic and venous pressure measurements on a number of the patients were consistently normal and were, therefore, omitted from later members of the series. The methods of study which were found to be more helpful were:

Lymphangiography of the Skin. The highly diffusible dye Patent Blue V was used in the way described by Hudack and McMaster.⁶ An intradermal injection of about 0.3 ml. of 11 per cent aqueous solution was made in each case. The interpretation of this test has been discussed elsewhere.⁷ A network of dilated lymphatics was shown in every case of lymphoedema. It was more widespread and marked than in cases of edema due to other causes such as cardiac failure. It was found also in many lymphoedematous patients that an injection into the skin of a contralateral and apparently normal limb showed a less marked but still definitely abnormal dilatation of lymphatics. This showed an abnormality of the lymphatic circulation to have been present, although it could not be detected by clinical examination.

Deep Lymphangiography at Operation. The development of this method and its use have been fully described elsewhere.⁷ Just before operation 2 to 3 ml. of 11 per cent Patent Blue solution is injected under the skin and into the muscles of the limb at a point distal to the site of operation. The site of injection, usually the foot, is vigorously massaged and the limb moved for a few minutes. During the course of subsequent dissection, lymph trunks filled with blue-green dye are found, usually lying near the deep veins. The normal lymph trunks in human limbs are about 1 mm. in diameter. A beaded appearance due to the presence of valves can often be seen.

* Submitted for publication October, 1953.

The results of this exploratory type of lymphangiography in lymphedematous patients compared with those in a control group are shown in Table I.

TABLE I. Results of Deep Lymphangiography.

	Control Series	Patients with Lymphedema
Number of limbs.....	18	8
Lymph trunks seen?.....	16	6
Enlarged?.....	0	6
Normal flow of dye?.....	16	1

TABLE II. Protein Content of Lymph from Legs of 8 Patients with Lymphedema.

Severity of Edema.	Total Protein (Gm. %)
Mild	1.0
Moderate	2.75
	3.0
	1.0
Severe	1.75
	2.25
	3.4
	5.0
	Average 2.5
Normal human skin (Drinker)	0.69

TABLE III. Absorption of Protein from Limb.

Appearance of protein (tagged with I¹³¹) in blood after subcutaneous injection

Patient	Rise of activity in BLOOD (10 ⁻⁴ % dose/ml./hr.)	Diagnosis.
J. R.	8.5	Normal leg.
F. S.	6.0	Normal leg.
E. K.	0.76	Lymphedema (leg)
G. M.	0.48	Lymphedema (leg)
V. S.	0.24	Lymph obstruction (arm) (malignant l.g.s.)

The control group consisted of patients undergoing operations on the limbs in the region of deep vessels which allowed some search to be made for the colored lymphatics. Some of the operations were for simple tumours such as lipomata, others for varicose veins or for the post phlebotic syndrome. There was an opportunity to look for lymphatics at operation in eight lymphedematous patients. Dilated lymph trunks were found in six, but only one of them contained dye. The others were filled

with clear fluid. Dilation of the lymphatics must inevitably have led to incompetence of the valves, particularly as some of these vessels were 1 cm. or more wide. Failure to transmit the dye was confirmatory evidence of incompetent valves and retarded flow of lymph.

No deep lymphatics were seen in two of the lymphedematous patients in Table I. Microscopy of the subcutaneous tissues subsequently showed the presence of prominent dilated lymphatics. All eight of these patients were, therefore, shown by one method or another to have abnormally dilated lymphatics.

Further information about the efficiency of lymphatic valves in lymphedema is supplied by cases of Chylous reflux. The chyle acts as a visual tracer. The following case was particularly instructive.

CASE REPORT

Case 1. The subject was a female, with spontaneous swelling of the left leg at age 13. She developed ascites and white vesicles on thigh and vulva at age 40 (Fig. 4). Ascitic fluid and fluid withdrawn from the lower leg resembled cream and had high fat and protein contents (Fig. 5). Laparotomy was performed at age 42. There were huge lymphatics filled with chyle, which extended from the diaphragm to the pelvis. A fistula from one of these opened in the pelvis. It was closed with gelatine foam and the trunk ligated. The ascites remained cured 18 months after operation and the vesicles had gone. The leg was still swollen.

This case showed incompetence of the lymphatics over a wide extent; from cisterna chyli to leg. No mechanical obstruction to the lymphatics could be found.

Roentgen Ray Lymphangiography. It has been possible, in a few cases where large lymphatics have been exposed at operation, to insert a small cannula and inject diodone solution. Radiographs have then outlined the lymphatics.

Figure 6 is a radiograph made a few seconds after 10 ml. of 50 per cent diodone was injected into the distal cut end of a dilated lymphatic lying near the great

saphenous vein and widely and with foot, showing competent or no ml. of diodone passed through the thigh. A f



FIG. 1. Blue dye, blue-green

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saphenous vein. The solution passed rapidly and without resistance down to the foot, showing that the valves were incompetent or nonexistent. An injection of 30 ml. of diodone injected upwards (Fig. 7) passed through enormous lymphatics in the thigh. A film of the pelvis showed them

dilated and tortuous lymphatics in the leg.

Microscopy of Excised Tissue. Section and microscopy of edematous subcutaneous tissue excised in the course of operations on eight of these patients showed the presence of dilated lymphatics in every case. The prominence and degree of dilatation



FIG. 1. Enlarged photograph of normal axillary lymph trunk (arrow) filled with Patent Blue dye., 2.5 ml. of 11 per cent solution injected under palmar skin 20 minutes earlier. The blue-green color renders it conspicuous *in vivo*.

to extend upwards through the femoral canal and onwards into the abdomen. There was no evidence of a block, and the ease with which the liquid flowed suggested that no obstruction could exist.

In another, less severe case of lymphedema, a dilated lymphatic was found on the dorsum of the foot beside a vein which had been exposed for phlebography (Fig. 8). Diodone injection showed numerous

of the lymphatics was roughly proportional to the severity of the edema. This method gives no direct information about the function of the lymphatics, and by itself would be but cautiously received. Taken together with the findings of the other methods, it confirmed that the lymphatics were abnormal.

Tissue Fluid Analyses. The protein contents of fluids from the legs of eight pa-

tients with lymphedema are set out in Table II. The fluid was obtained by direct puncture, using a Southey's tube, or during operation from the tissues or the dilated lymph trunks. Specimens contaminated with blood were discarded. Drinker and Yoffey² consider that lymph and tissue fluid

was 2.5 Gm. per cent, figures which might be expected to occur in the presence of lymph stasis. The figure of 0.69 Gm. per cent for lymph from normal human skin is that cited by Drinker and Yoffey.²

Studies of the Absorption of Radio-active Marked Protein from the Limb. Informa-

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FIG. 2. Enlarged photograph of normal lymph trunks (arrow) lying on popliteal artery. 2.5 ml. 11 per cent Patent Blue solution injected subcutaneously 30 minutes earlier. The blue-green color of the dye is conspicuous *in vivo*.

are approximately identical in composition and so these specimens may fairly be regarded as representing samples of lymph in each case.

The protein concentration was found to be roughly proportional to the clinical severity of the edema. The range was from 1 to 5, and the average of the eight cases

tion about the lymphatic circulation may be obtained by injecting small amounts of the patients serum protein, marked with radio-active iodine,³ under the skin of the affected limb. Its absorption may be studied by counting the radioactivity over the site of injection and also by noting the rate of its appearance in samples of venous

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blood withdrawn at intervals. A detailed account of these studies is to be published separately.⁸

In Table III the rates of absorption of protein injected in this way under the skin of two normal subjects are compared with the rate in two patients with lymphedema

large, dilated, incompetent lymphatics exist in the limbs of patients with lymphedema. Tissue fluid analysis and tracer studies with marked protein have confirmed that the lymphatic circulation is extremely sluggish in the swollen areas. No evidence of any anatomical obstruction in the lymph



FIG. 3. Dilated popliteal lymphatics in a case of lymphedema (black thread underlying). They are filled with clear fluid and dye is not transmitted as in normal control cases.

and found to be approximately ten times as great. Both normals and patients were ambulant during the tests. The rate of protein absorption in a patient with severe lymphatic obstruction due to secondary carcinoma of axillary lymph glands is also shown for comparison. It is even slower than in the cases of idiopathic lymphedema.

DISCUSSION

The Abnormal Lymphatics. The evidence from our studies has shown that

vessels was ever found. In the light of these findings, it was interesting to read that Servelle¹³ had studied similar patients by injections of radio-opaque dyes. He also found dilated incompetent lymphatics but postulated a block in the region of the femoral canal because the dye was not shown above the thigh.

Homans, Drinker and Field in 1934,⁵ after studies using the dye Trypan Blue and exploratory operations, wrote this about the causes of clinical lymphedema:



FIG. 4. White vesicles on thigh of patient with chylous reflux described in text.

"A malformation or varicosity of the lymphatics may be present. Yet there is no actual evidence in support of this conception of varicose lymphatics, and it is rather more likely that there is an incomplete development of the lymphatics in such cases." The data from our studies and those of Servelle supply the missing evidence.

The Cause of the Lymphatic Abnormality. The way in which the lymphatics have become incompetent and dilated is largely a matter for discussion, as little direct evidence exists. A temporary obstruction to the outflow of lymph from the limb might cause a persistent dilatation and incompetence of lymph trunks. Animal experiments show that this is possible. We have produced, in the rabbit, a temporary lymph obstruction by excision of pelvic lymph trunks and nodes. Although a collateral lymph circulation soon developed, the lymph trunks of the thigh were left in a permanently dilated state. Infection has

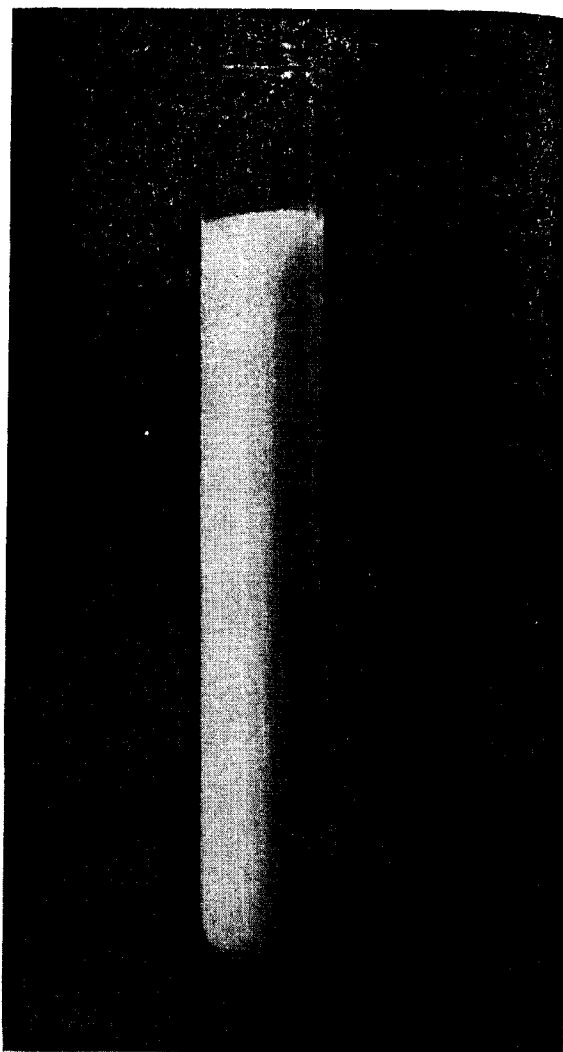


FIG. 5. Chyle obtained by puncture from leg of patient described in text.

been frequently postulated as a cause of lymphatic obstruction and Servelle found that most of the cases in his series¹² started with infection of a minor wound. This has definitely not been so in our patients. Only six of the 15 ever had any evidence of inflammation in the limb or lymph nodes at any time and in those that did the lymphedema was already established before the inflammation happened. It has been quite evident that the inflammation was a purely secondary happening.

Alteration in the permeability of the blood capillaries to protein might result in the formation of a protein rich tissue

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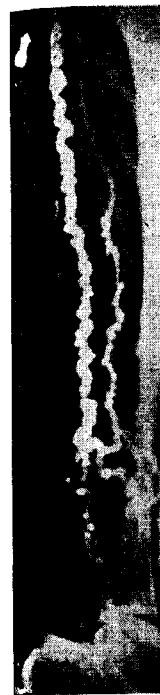


FIG. 6. R phatics in ca text).
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fluid. If this continued over a long period of time it might be supposed that the lymphatics would become hypertrophied and dilated through constant filling and distension. We have studied this possibility in the rabbit by maintaining a protein rich edema in the hind limb by daily injections

existed with the lymphatic changes, but in most others the late age at which symptoms first appeared was against the theory. The changes in the structure of the lymphatics might alternatively be regarded as a benign new growth, a diffuse lymphangioma. The malignant change which took place in

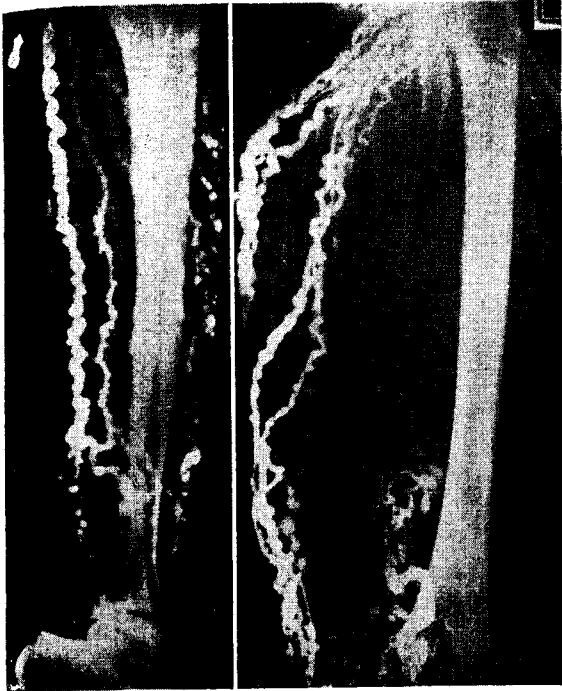


FIG. 6

FIG. 7

FIG. 6. Retrograde flow of diodone in lymphatics in case of lymphedema (description in text).

FIG. 7. Upward flow of diodone in lymphatics in case of lymphedema (description in text).

of plasma over a period of time. No significant dilatation of the lymph trunks took place over periods of three to four weeks. It may be objected that this time was not long enough to be comparable with what might happen in patients, but technical difficulties prevented maintenance of the edema for longer periods. No final verdict is possible until the difficulties can be overcome, but the limited evidence is against the theory.

Congenital malformation of the lymphatics is another explanation. This was a most credible idea in one patient in whom malformations of the blood vessels co-



FIG. 8. Dilated translucent lymphatic (black threads, right) on dorsum of foot. Injection of diodone showed dilated lymphatics in leg. A vein (white threads) lies to its left.

a case reported by Martorell⁹ would support such an idea. A final explanation of the cause of the lymphatic dilatation will not be possible until further evidence is available.

Surgical Treatment. Operations have been designed in the past to bridge theoretical obstructions to the lymphatic return. Gillies' operation⁴ aimed at diverting lymph from the lower limb into the axillary drainage area through the lymphatics in a skin pedicle graft inserted from thigh

to abdomen. The success reported from these operations is likely to have been due to the insertion of normal lymphatics with competent valves rather than to bridging an area of obstruction.

A different approach is to treat the incompetent lymph trunks like varicose veins and tie them so that the lymph returns by alternative, and it is hoped more competent, channels. We have treated one patient in this way by ligation of lymphatics at the lower end of the femoral canal. It was followed by temporarily increased swelling of the scrotum. The edema of the thigh and leg was unaffected. In another patient, chylous reflux into the thigh was stopped by ligation of a pelvic lymph trunk, but again without improvement in the edema of thigh and leg. Servelle has also reported successful treatment of chylous reflux by lymphatic ligation.¹³

The operation which we have found most useful has been a superficial lymphangiectomy. The edematous subcutaneous tissue is excised and the muscles covered by free skin grafts. The principle of this was described by Charles in 1912.¹ It has always been possible in our cases to use the original skin of the limb for the graft in the way described by McIndoe in 1950.¹⁰ Watson has recently reported good results from this method.¹⁴ It is, however, a major undertaking, and should not be done unless the patient is severely handicapped.

SUMMARY

Patients with idiopathic lymphedema of the lower limbs have been studied by methods which included exploratory lymphangiography with Patent Blue dye, roentgenologic lymphangiography, tissue fluid analysis and tracer tests with radio protein. Lymphatic stasis was shown to exist. The lymphatics were dilated, valveless and incompetent. No direct evidence of obstruction could be found.

The etiology of the disease and its surgical treatment are discussed in the light of these findings.

ACKNOWLEDGMENTS

We are grateful to Professor Sir James Paterson Ross, Mr. D. J. Robertson and Dr. J. E. M. Connolly for clinical help and advice; to Professor J. Rotblat, Dr. E. Rollinson and Mr. G. E. Francis for their part in the isotope studies; to Miss M. Morley for technical help, to the Photographic Department of St. Bartholomew's Hospital, and to colleagues who have kindly referred patients to us.

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