LYMPHANGIOGRAPHY — ITS TECHNIQUE AND VALUE

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The place of lymphangiography in the study of the lymphatic system is now well established. The technique of this investigation is fairly simple and is based on the original description of modern lymphangiography by Kinmonth and Taylor.[1] The technique has been modified by various clinics and the technique used at this hospital will be described.

This investigation can be done under local or general anaesthesia. Most of our patients were investigated under local anaesthesia in the operating theatre. This procedure could also be performed in the ward or X-ray department.

MATERIALS AND METHODS

Materials Required

(a) *A diffusible dye such as patent blue violet.* A solution of 5-11% is used. Patent blue violet powder is readily available in this country and it is a simple matter to make up the required solution. This dye is readily taken up by the lymphatic vessels, which can then be dissected out in readiness for intralymphatic injection of a radiopaque substance.

(b) *Radiopaque material for intralymphatic injection.* The material used here is Lipiodol ultra fluid 38%.* This oily solution is available in ampoules of 5 ml. and 10 ml. This preparation has been found to be extremely satisfactory in demonstrating the lymphatic vessels and lymph nodes, particularly para-aortic nodes and even the thoracic duct.

(c) *A needle of small calibre with a polythene and 'luerlock' connection for injecting the dye into the lymphatic.* A special needle-polyethylene tubing unit is available from Dubernard S.A.† Here we have made our own needle combination. A 26 luerlock needle is cut off squarely about ¼-½-inch from its base. To this an 8-inch-long polythene PE 20 tube is attached and at its distal end the remains of the No. 26 luerlock needle is inserted. This unit is very convenient and easy to use.

(d) *An automatic injector.* We use the Braun apparatus as demonstrated, with a Y-connection or two syringes so that both legs can be injected at the same time.

(e) *A basic set for dissection.* No pre-operative preparation is required, except for patients with lymphoedema. Here it is helpful if the oedema can be diminished to some degree by elevation of the foot of the bed and bandaging of the limbs for a period of 2 or 3 days.

Technique

The following technique is used for demonstrating the lymphatic vessels of the lower limbs, the inguinal, iliac and the para-aortic glands:

Infiltration. After normal skin preparation 0.2 ml. of the patent blue violet is injected into the medial 2 digital clefts of the feet (Fig. 1). It is convenient to add local anaesthetic to the dye, or local anaesthetic can be injected before injecting the dye. The bases of the toes are massaged to aid the absorption of the dye into the lymphatics. In Whites the lymphatics can often be seen outlined on the dorsum of the foot. After infiltrating the area with local anaesthetic, a longitudinal incision is made over the first metatarsal bone, or over a convenient lymphatic, if it can be seen (Fig. 2). This incision must not be too deep in order to avoid damaging the lymphatic vessels. The skin is dissected off the subcutaneous tissue and normally the lymphatics are easily visualized. Several lymphatics are usually seen in a normal limb, but in the cases of primary lymphoedema one or two thin lymphatics are found.

*Obtainable from Laboratoires André Geurbet & Cie, Saint-Ouen, Paris, France.
†Dubernard S.A., 26 rue H. Jamot, Sannois (S-et-O), France.

Dissection. It is important not to isolate the whole lymphatic vessel so that one is left with a little string of tissue. It is better to dissect the lymphatic free with some perilymphatic tissue which anchors the vessel, making injection much easier. Injection is also aided by distending the lymphatic. This can be done by placing a small bulldog clamp proximally and by massaging the base of the toes. It is then fairly simple to insert the needle (Fig. 3) ; as soon as the needle is in the lymphatic, the blue dye pushes back into the polythene tubing. The needle can then be tied into the lymphatic or a small bulldog can be used to anchor the needle. The polythene tubing is then attached to the automatic syringe and the dye injected. With correct placement of the needle there is no leakage and one can often see the little bubbles of air traversing the lymphatic vessel. For demonstrating the intra-abdominal glands it is advisable to inject dye into both legs. At the same sitting the other foot is similarly dissected and a needle placed into position in readiness for the injection of ultra fluid, employing the Braun automatic syringe (Fig. 4).

Injection and X-ray. The volume of dye to be injected is important. For an adult the maximum dosage is 14 ml. and it is proportionally smaller for children. Gough *et al.*[2] recommended 0.25 ml./kg. body weight. Cases have been reported, especially in children, where pulmonary fibrosis has occurred with even fatal results. We usually set the machine to inject 12 ml./hour. Once the dye has been injected the first X-rays are taken, i.e. a posterior-anterior exposure of the pelvis, and a posterior-anterior and lateral exposure of the abdomen and chest. An hour later this is repeated and again in 24 hours' time. The patient is asked to walk around before the 24-hour film is taken. This gives maximum filling of the abdominal lymph nodes. By this time the lymph vessels are empty of dye and the dye is concentrated entirely in the lymph glands.

If a venogram should be desired, a vein can be cannulated through the same incision as used for the lymphogram. To demonstrate the glands in the axilla, patent blue violet is injected into the lateral three digital clefts of the hand and a lymphatic dissected out on the dorsum of the hand. About 5 ml. of radiopaque dye is sufficient in an adult.

Complications[3]

Complications are rare and usually minor. The following may arise:

1. *Pain* between the toes and in the foot can occur.
2. *Infection* is rare, but does occur occasionally.
3. *Discolouration of the skin.* Local discolouration remains for some time, which is not really a complication in the feet, but when the upper limb is studied, discolouration of the hands is unsightly. It is just as well to remember that the whole patient sometimes becomes blue because of the patent blue violet injection. This blue discolouration usually disappears within 24 hours. The urine is usually discoloured blue for the same period.
4. *Hypersensitivity* reactions to the ultra fluid oil have been reported, but have been of minor degree.
5. *Oil embolism.* The most important region affected is the lungs. Several cases of pulmonary fibrosis have been reported, as well as cases of fatal pulmonary oedema. It is important not to exceed the normal dosage of the ultra fluid oil and one should be cautious in using the technique in patients with decreased pulmonary function. Gough *et al.*[2] quote a case where a child of 30 kg. was infused with 28 ml. of ultra fluid Lipiodol and died of pulmonary oedema on the 4th postoperative day. Their experiments on rabbits showed that a dose greater than 1 ml. per kg. was usually fatal, due to fat embolization in the pulmonary arteries.
6. *Lymphatic obstruction.* The ultra fluid oil remains in the lymphatic glands for several weeks to several months, but very few cases of lymphatic obstruction secondary to this have been reported.

THE VALUE OF LYMPHANGIOGRAPHY

Lymphangiography has been proved to be of value in the differential diagnosis of certain pathological conditions. It may save a patient an unnecessary operation or be of use to determine the form of treatment that should be adopted. It can also help to determine the progress of a patient during follow-up studies. Lymphangiography has proved worth while in studying the following conditions:

1. Lymphoedema

In order to understand the diagnostic possibilities of lymphangiography in lymphoedema it is useful to review

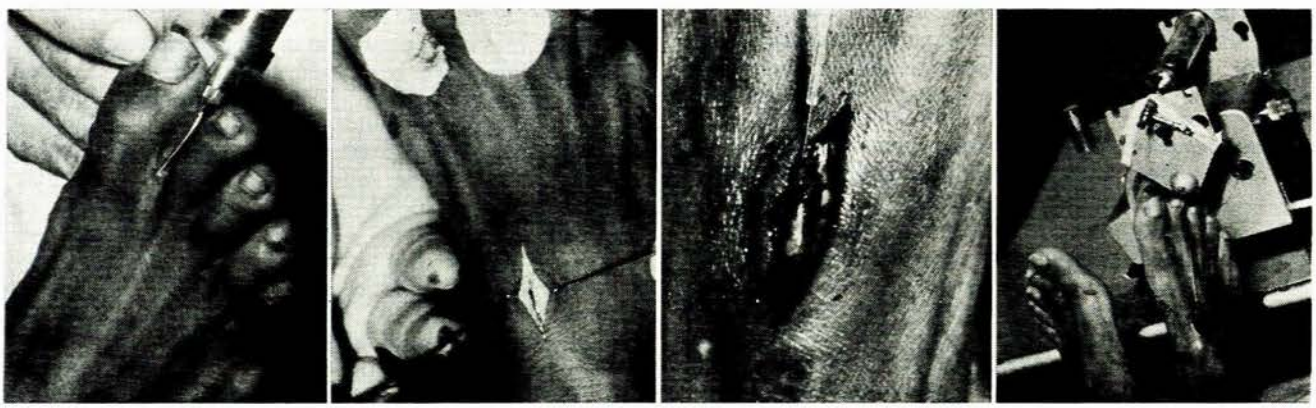

Fig. 1. Injection of patent blue violet into digital cleft. Note that the injection is superficial. *Fig. 2.* The blue-coloured lymphatic vessel is seen. *Fig. 3.* Needle tied into lymphatic. *Fig. 4.* Both feet are being injected simultaneously with Lipiodol ultra fluid, employing the Braun automatic syringe.

this condition in the various forms it may present. Taylor[4] proposed the following classification of lymphoedema:

(a) *Primary lymphoedema.*

(b) *Secondary lymphoedema* owing to interference of lymphatic function by the following acquired lesions:

(i) neoplastic invasion;
(ii) surgical excision or radiotherapy;
(iii) inflammation or filariasis; and
(iv) motor paralysis of the part.

Primary Lymphoedema

Primary lymphoedema is due to a lymphatic fault which can be divided into *three* main types:

(a) *Aplasia.* Here no formed lymphatics are found and this abnormality accounts for about 17% of people with primary lymphoedema.

(b) *Hypoplasia.* This is the most common variety and accounts for about 60% of cases with lymphoedema. On lymphangiography only one or two thin lymphatic trunks are visualized, as compared to a normal limb, where several bifurcating trunks are seen.

(c) *Varicose lymph trunks.* This accounts for about 15% of cases of lymphoedema. Lymphangiography shows many dilated lymph trunks which are tortuous and this variety may be associated with congenital arteriovenous fistulae.

Primary lymphoedema can also be divided into *three* clinical groups:

(a) *Lymphoedema congenita* (10%). The onset of lymphoedema is usually at birth and the lymphatic fault is usually aplasia.

(b) *Lymphoedema praecox* (80%). The age of onset is before 35 years and the abnormality is usually hypoplasia or the varicose type of lymphatic.

(c) *Lymphoedema tarda* (10%). The age of onset is after 35 years and the lymphatic fault similar to lymphoedema praecox.

Secondary Lymphoedema

Secondary lymphoedema is often not a diagnostic problem as the cause is usually apparent, but cases are seen where the diagnosis is not certain and lymphangiography is found to be of particular value.

Findings on Lymphangiography

In *primary lymphoedema* one either finds no lymphatic vessel, or, if a lymphatic can be cannulated, one sees one or two thin radiopaque lines.

In the *varicose type,* tortuous dilated trunks are seen with dermal backflow in some patients.

In *secondary lymphoedema* the lymphatics are relatively normal and the main trunks stop at the site of obstruction. In addition there is a backflow of dye in the dermal lymphatics. Occasionally cases are seen where a diagnosis between venous and lymphatic obstruction has to be made and in these patients it is convenient to do a lymphogram and a venogram at the same time.

2. Metastatic carcinoma

Wallace *et al.*[5] found this technique of value in studying metastases from the breast and testis. Gould and Schaffer[6] present 8 representative cases where lymphangiography was found to be of value in assessing, for instance, the completeness of a lymph gland block dissection, and this technique has been used by many workers in assessing the completeness of gland clearance in radical mastectomy.

In clinics where a para-aortic and pelvic block dissection is performed for carcinoma of the testis, this technique is used to assess the completeness of clearance.

Lymphangiography has also demonstrated how difficult it is to perform a complete para-aortic gland clearance. As the glands retain the dye for several weeks, the radiotherapist can be guided in applying radiotherapy to the glands not resected.

Lymphangiographic findings in carcinoma of the lymph nodes.[5] There is an increase in the number and size of the nodes and one sees irregular filling defects in the margin of the nodes, giving a moth-eaten appearance. Where there is extensive metastatic involvement the nodes are not visualized and the lymphatic vessels are seen to circumvent the nodes.

Sheehan *et al.*,[3] after studying 20 cases of metastatic carcinoma, could demonstrate changes in only 8 of these, but there were certain shortcomings: when the metastases were small, they were not demonstrated; nodes completely replaced by metastases could not be demonstrated except where they were displaced by lymphatic vessels; where the nodes showed filling defects it was not certain whether this was due to incomplete filling or inflammatory change. This view is supported by other authors.

Schaffer *et al.*[7] state that lymphangiography was of less value in the detection of metastatic carcinoma than when compared to the lymphoma group of diseases.

Ditchek *et al.*,[8] trying to evaluate the procedure in early metastatic lymph node involvement, studied 16 normal subjects and found defects in the inguinal, femoral, iliac and para-aortic glands. These filling defects were thought to be due to areas of fibrosis resulting from old inflammatory disease, and they came to the conclusion that this technique was of some limited value. Gould and Schaffer[6] state that filling defects occur in normal nodes and add that inguinal and femoral nodes are difficult to interpret as inflammatory changes so often occur. In inflammation the nodes are typically large, ragged and usually do have filling defects with interruption of the cortical outline. Usually these defects are not as sharply defined as in carcinoma, but in general the interpretation can be difficult.

3. The Lymphomas

Many authors[2, 3, 5, 7, 9, 10] stress the value of this technique in studying lymph nodes involved by the lymphomas. Lymphomatous nodes have typical radiological appearances. The nodes are enlarged, have intact borders and appear foamy. There is coarsening and exaggeration of the normal reticular pattern, with subcapsular accumulation of contrast medium. In Hodgkin's disease the nodes are enlarged, and sometimes scattered areas of moth-eaten appearance occur. With experience nodes involved by Hodgkin's disease, lymphosarcoma, reticulum cell sarcoma and leukaemia can be identified.

This technique is important in assessing the extent of nodal involvement in the lymphomas. Patients presenting with involvement of a single group of glands, e.g. neck, axillary or inguinal glands, can be investigated by this

Fig. 5. Enlarged inguinal, iliac and para-aortic glands, typical of leukaemia. *Fig. 6.* Enlarged inguinal, iliac and retroperitoneal glands with foamy appearance of Hodgkin's disease. *Fig. 7.* Treatment with Endoxan resulted in a shrinkage of the glands.

technique to decide whether external iliac and para-aortic glands are involved. Involvement of these impalpable glands is important in treatment.

Another factor of importance is the fact that the dye remains in the glands for some weeks and their shrinkage in size can be assessed after treatment with radiotherapy and/or with cytotoxic agents. It also guides the radiotherapist to the site to which radiotherapy should be concentrated. Sheehan *et al.*,[3] for example, found retroperitoneal glands involved with lymphoma in 13 unsuspected cases and used this as a guide to concentrate radiotherapy in the exact areas involved. Lee *et al.*[10] used a combination of inferior venacavography, intravenous pyelograms, plus lymphangiography to assess the para-aortic and external iliac involvement of lymph nodes in the lymphomas. With this method, and by using Peters' staging, they could classify the patients more accurately into either Peters' type I, II or III. Peters[11] uses the following staging:

Stage I. Involvement of a single site or lymphatic region.

Stage II. Involvement of two or three proximal lymphatic regions. This is subdivided into:

(a) With no symptoms of generalized disease.
(b) With symptoms of generalized disease.

Stage III. Involvement of two or more distant lymphatic regions.

One of Peters' conclusions was that the staging of the disease is an important factor in the prognosis of Hodgkin's disease, but after careful consideration and evaluation there was still a 35% error in staging. As a matter of interest, the 10-year survivals in the study of 291 cases were: stage 1 58%; stage II 35%; and stage III 2%.

Lee *et al.*[10] thought that with their combined technique they could come to a better conclusion as far as staging is concerned and found that, after studying 186 patients, 30 out of 63 patients with a clinical stage I or II Hodgkin's disease had retroperitoneal lymphomatous involvement. Only 3 out of 40 patients with stage I and stage II lymphosarcoma or reticulum cell sarcoma had localized disease.

Other conditions have been studied by lymphangiography, e.g. retroperitoneal fibrosis. Clouse *et al.*,[12] in a study of 3 cases of retroperitoneal fibrosis, found collateral filling and reflux of the contrast medium into the lymphatic channels not normally visualized, non-visualization of lymphatic channels above the first lumbar vertebra and irregular filling defects in the lymph nodes. They stress that this technique is important to assess the extent and even to make the diagnosis of retroperitoneal fibrosis.

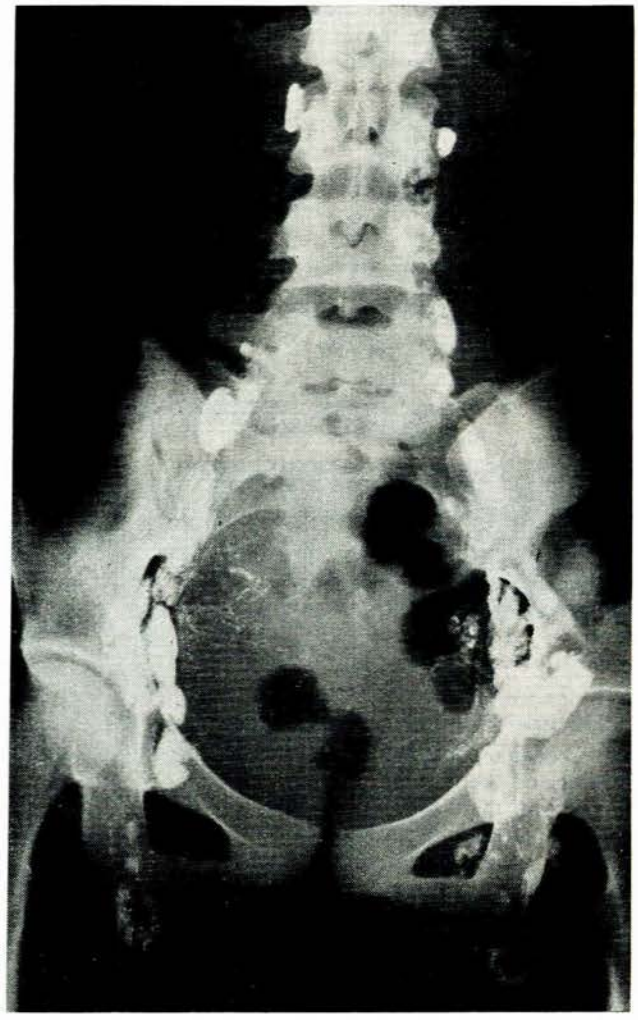

Fig. 8. Enlarged external iliac glands with some obstruction to the lymphatic flow — note streaking of lymph vessels in pelvis.

This procedure can also be used to investigate lymphangiomas, thoracic duct physiology and abnormalities, chylous effusions, etc.

CASE REPORTS

Case 1

A White male, aged 74, presented with anaemia and generalized lymphadenopathy, involving supraclavicular, cervical, axillary and inguinal glands.

Blood examination. Hb. 6·4 G/100 ml.; WBC 544,000/cu. mm.; lymphocytes 98%; polymorphs 2%.

The bone marrow showed signs of chronic lymphatic leukaemia. A lymphogram was done to show the inguinal, iliac and para-aortic glands (Fig. 5). All the glands were found to be enlarged and had the typical appearance of leukaemia. As a therapeutic trial in this patient 25 mg. of Methotrexate was injected intralymphatically. No untoward reaction occurred locally or in the regional glands. The concept of intralymphatic perfusion with cytotoxic agents will be discussed later.

Case 2

A non-White male, aged 26, presented with lymphadenopathy involving both inguinal regions, the neck and axillae. A biopsy was performed on a neck gland and the diagnosis of Hodgkin's disease was confirmed.

The lymphogram (Fig. 6) showed enlarged inguinal, iliac and retroperitoneal glands with the typical foamy appearance of Hodgkin's disease.

An X-ray of the chest showed involved mediastinal glands. The patient was treated with Endoxan. Two months later straight X-rays of the pelvis and abdomen (Fig. 7) showed a shrinkage of the glands as a result of treatment.

Fig. 9. Enlarged right inguinal glands with partial replacement of the glandular tissue in the most distal gland.

This patient demonstrates the value of lymphangiography in a follow-up study of Hodgkin's disease. In addition it showed that the para-aortic glands were involved and treatment directed in this area was then instituted.

Case 3

A non-White female, aged 21. Five months before admission she had undergone a laparotomy in another hospital for abdominal pain and jaundice. Tuberculous peritonitis was diagnosed.

On admission she showed a recurrence of jaundice and complained of abdominal pain and distension.

On examination the patient was thin, anaemic, with enlarged neck, axillary and inguinal glands. The abdomen was distended. The liver was enlarged and there was a vague mass in the left iliac fossa. A left inguinal gland was taken for a biopsy and the diagnosis of tuberculosis confirmed.

Lymphangiography was performed to decide whether intrapelvic and para-aortic glands were involved. Lymphangiogram (Fig. 8) showed enlarged external iliac glands with some obstruction to the lymphatic flow, as evidenced by the streaking of lymphatic vessels in the pelvis. In the region of L.2 on the left two glands appeared only partly filled, probably due to caseation. Some para-aortic glands failed to fill. The patient's condition deteriorated and she died before a laparotomy could be performed.

At autopsy it was found that she had enormous caseating tuberculous glands in the porta hepatis, causing an obstructive

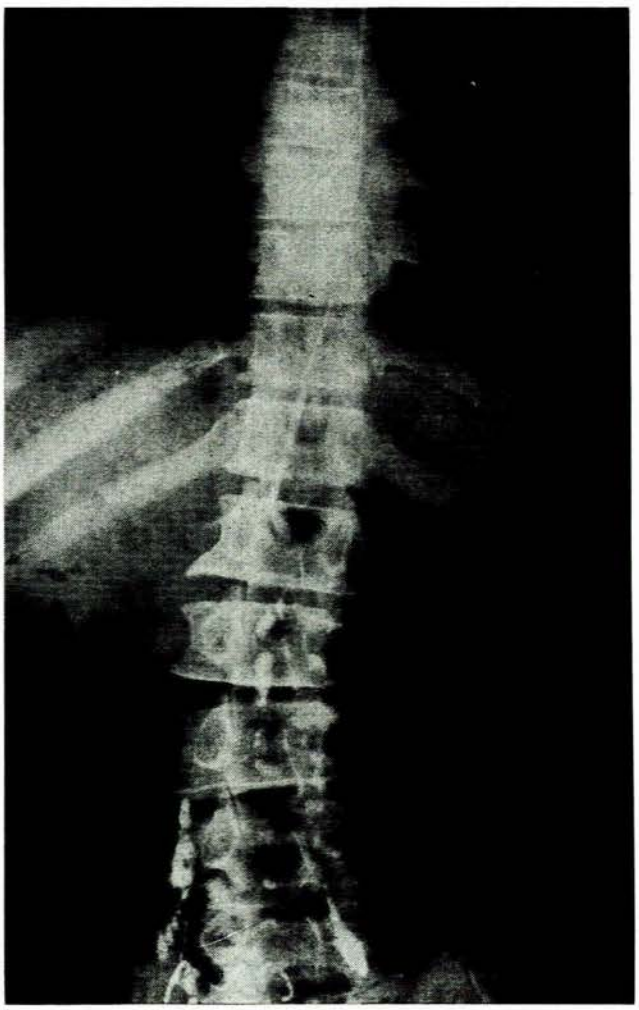

Fig. 10. Normal para-aortic glands, cysterna chyli and thoracic duct.

jaundice as well as glands in the para-aortic region and in the pelvis.

The value of the investigation in this patient was to show generalized involvement of the lymph nodes and should have led one to the correct diagnosis of her jaundice since it would have been reasonable to assume that the glands in the porta hepatis could be involved.

Case 4

A non-White male, aged 60, presented with a carcinoma of the penis, with enlarged right and left inguinal glands. The right glands were definitely larger than the left and it was a thought that they were involved with metastases.

A lymphangiogram (Fig. 9) showed enlarged right inguinal glands with partial replacement of the glandular tissue in the most distal gland visualized. It also showed non-filling of some higher inguinal and possibly lower external iliac glands on the right side. The para-aortic glands definitely appeared normal and it was possible to see the cysterna chyli and the thoracic duct on another X-ray plate (Fig. 10).

After amputation of the penis, a bilateral block dissection was done of the inguinal glands and the external iliac glands explored and some removed for histology. All the glands proved to be negative for metastases.

The value of lymphangiography in this case was to show non-involvement of the external iliac glands as seen on this investigation. This case also demonstrates one of the difficulties in interpreting the radiological findings. The enlargement and defects found in the right inguinal glands were due to the change caused by secondary inflammation and not by carcinoma. The non-filling of some glands is not necessarily significant. Those glands may not exist at all and one should not assume that the glands should be bilaterally equal.

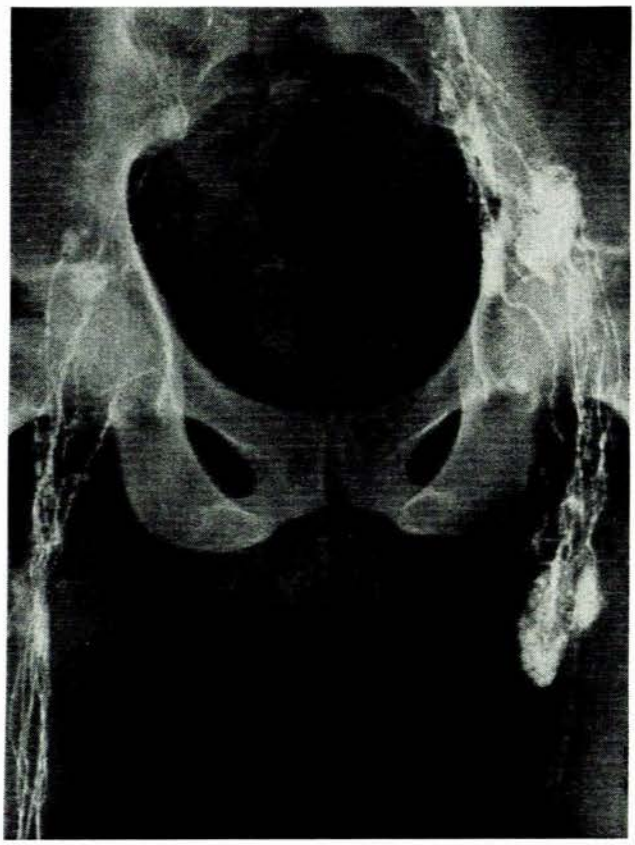

Fig. 11. Enlarged left lower and upper inguinal glands.

Case 5

A non-White male, aged 24, presented with a *Nocardia* infection of the left foot (Madura foot). Clinically it was thought that the fungus had spread to the inguinal glands. A lymphangiogram was performed and showed very much enlarged left lower and upper inguinal glands (Fig. 11) with normal para-aortic glands (Fig. 12). With some imagination one could possibly think that foci or fungi were present in the left inguinal glands according to these lymphangiographic pictures. The glands were removed surgically and found to be free of fungus.

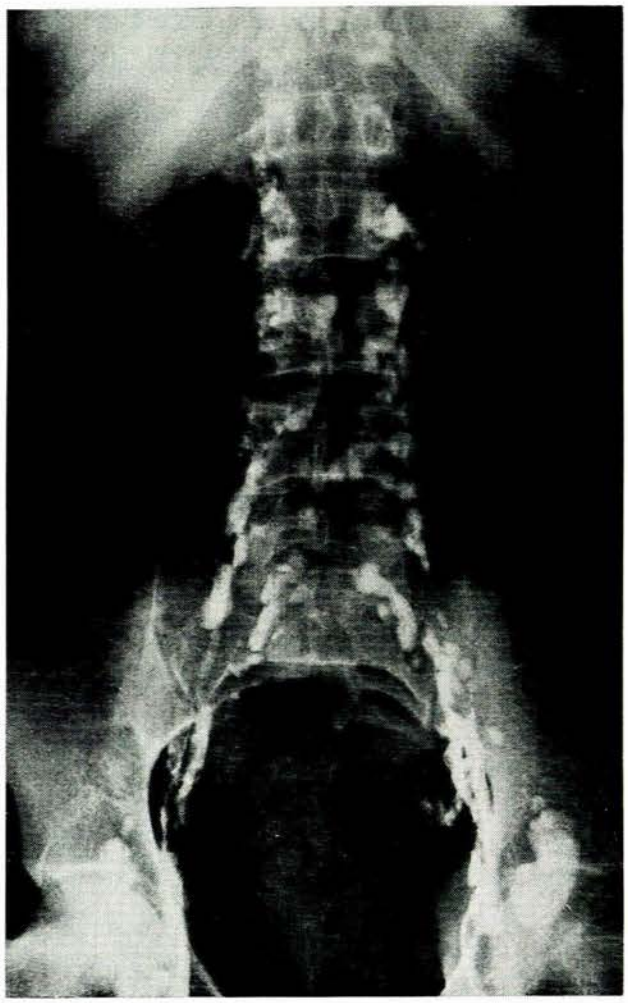

Fig. 12. Normal para-aortic glands.

Case 6

A non-White male, aged 60, presented with acute left renal pain 2 weeks before admission.

On examination a firm, tender mass was found in the left loin. All special investigations, including a barium meal, an IVP, etc., were normal. However, there was one striking abnormality, viz. the platelet count of 1½ million/cu.mm. Bone-marrow examination suggested a thrombocytosis. Since this condition occurs in the lymphoma group of diseases, it was decided to do a lymphangiogram.

The *lymphangiogram* proved to be entirely normal. This enabled us to make a diagnosis of thrombocythemia (idiopathic thrombocytosis). The patient was treated with Myleran

and responded well. The value of lymphangiography in this case is obvious.

Case 7

A White female, aged 32, presented with a swelling of the right leg which had been present for 5 years. It was difficult to decide whether this swelling was due to lymphoedema or not, and a lymphangiogram was performed, showing a normal lymphatic pattern (Fig. 13). The venous system was then investigated and a deep vein thrombosis of the leg was found.

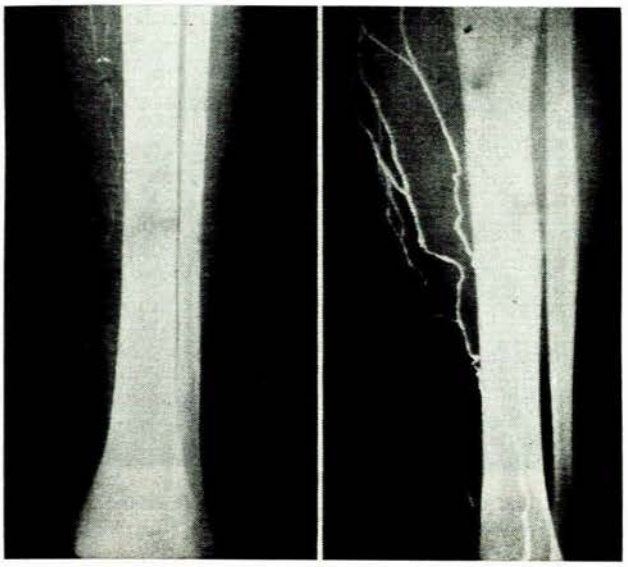

Fig. 13. Normal lymphatic pattern in the leg. *Fig. 14.* Varicose type of lymphatic abnormality in the leg.

Case 8

A non-White male, aged 40, complained of swelling of the right leg which had been present for 8 years. On examination the patient appeared to have primary lymphoedema. A lymphangiogram was performed and showed a typical varicose type of lymphatic abnormality (Fig. 14).

COMMENT

The case reports presented here serve as but a few examples of the value of lymphangiography in clinical practice. We have also found this technique of value in experimental surgery. A lymphangiogram on a dog, showing popliteal and retroperitoneal glands, is shown (Fig. 15). In a lymphangiogram on a rabbit a very large popliteal gland is visualized with a few efferent trunks running towards the pelvis (Fig. 16).

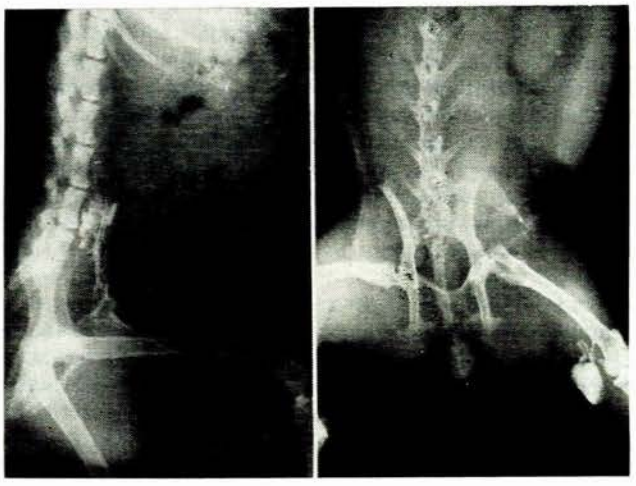

Fig. 15. Popliteal and retroperitoneal glands in a dog. *Fig. 16.* Large popliteal gland and efferent trunks in a rabbit.

The Concept of Intralymphatic Perfusion

This concept will shortly be discussed in greater detail; however, a few points bear mentioning here.

In experiments performed some years ago it was shown that intralymphatic perfusion was feasible. In dogs, after the injection of radioactive gold into a foot lymphatic, all the glands of that leg and the para-aortic glands were found to be radioactive. Since the gold is in colloidal form, it is taken up by the lymphatic tissue and is held there for some time.

In another group of dogs intralymphatic cytotoxic perfusion was done. The material used was mustine hydrochloride in a normal dose. The popliteal gland of a dog after infusion with Normal saline is shown in Fig. 17, and the opposite popliteal gland after infusion with mustine hydrochloride is shown in Fig. 18. It is obvious that all the lymphatic tissue has been destroyed. Gough *et al.*[2] and Jantet[13] have reported cases where they have injected radioactive gold intralymphatically in patients with malignant melanoma of the limbs to destroy melanoma cells which may be present as microscopic deposits in the draining lymph nodes.

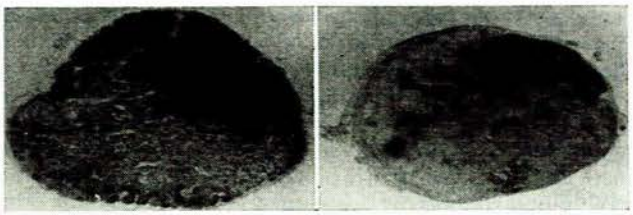

Fig. 17. Popliteal gland of a dog after infusion with normal saline. *Fig. 18.* Opposite popliteal gland after infusion with mustine hydrochloride.

CONCLUSION

The value of lymphangiography is obvious. It is a relatively simple method. The interpretation can be difficult, but with experience the pitfalls will be eliminated. The concept of intralymphatic perfusion is mentioned and on the basis of experimental work performed, is a feasible procedure.

I wish to thank Dr. R. L. M. Kotze, Medical Superintendent of the Karl Bremer Hospital, for permission to publish these case reports. I wish to express my gratitude towards Messrs. G. Mead and R. Cloete for technical assistance; to Mr. R. Ellis for the photographs and to the staff of the radiology department for their cooperation.

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