Papers and Originals

Lymphovenous Shunts in Man

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[WITH SPECIAL PLATE BETWEEN PAGES 586–587]

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Summary: Lymphovenous shunts have been detected in patients by lymphography with Ultrafluid Lipiodol. No shunts were found in patients with normal lymphatic systems. They were found in patients with lymphoedema, with lymph nodes involved by malignant disease, and in patients who had had surgical interruption of lymphatic pathways, either vessels or nodes. The total incidence of lymphovenous shunts in 700 lymphographic studies was 2·3%. The incidence in the various pathological groups was highest in those with obvious lymph node involvement.

In certain situations, particularly primary lymphoedema, the role of a lymphovenous shunt appears favourable to prognosis. In other situations a deleterious effect may be produced.

Introduction

Evidence of the existence of peripheral lymphovenous shunts collected from patients investigated by lymphography is presented here.

The occurrence of lymphatic to venous communications other than those at the end of the thoracic duct or at a neighbouring level have been argued for years. The general view, as voiced for example by Le Gros Clark (1958) when reviewing the subject, has been that they exist at peripheral level in certain animals such as dogs, cats, squirrels, and South American monkeys, but not in man. More recently Pentecost *et al.* (1966) have studied them in the dog, and Threefoot *et al.* (1963) in the human cadaver.

Studies in vivo in man have been comparatively few, but the existence of peripheral lymphovenous shunts has often been discussed since the development of clinical lymphography. Many of the references have been made in papers devoted to other and general aspects of lymphography. Often the existence of abnormal lymphovenous communications has been inferred from the demonstration of excessive amounts of contrast material in the lungs. Many of these instances could, however, be explained in other ways. The use of unusually large volumes of oil contrast medium might result in the pulmonary circulation receiving through the normal thoracic duct to venous connexions more oil than normally expected. Some patients, particularly elderly people, have a small capacity in their lymph system, so that the conventional volume of oil may soon fill the pathways and overflow through the normal thoracic duct route into the subclavian vein and thence reach the pulmonary circulation.

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There have, however, been a few instances where the evidence for lymphovenous shunting at an abnormally peripheral level in patients has been strong. Wallace *et al.* (1964) showed an example in the cervical region. Wolfel (1965) reported a case of a patient with seminoma with lumbar node metastases and evidence of oil entering the vena cava at this level. Marrocu and Cossu (1964) described shunting in the thigh of a patient with an endothelioma. Their evidence was supported by serial radiographs, though the actual exact site of the shunt was not apparent. Schaffer *et al.* (1963) published evidence suggestive of a shunt in the pelvis of a patient with stage III carcinoma of the cervix uteri.

These individual reports have been highly suggestive of the occurrence of lymphovenous shunting. It was thought that more definite evidence was needed of the existence of these shunts in clinical practice, careful examination and criteria being used. Some measure of their incidence was also considered important. To these ends the cases found in the clinical practice of this department over a number of years were collected and reviewed. It will be seen that more conclusive evidence has been collected of their existence. Their physiological and pathological significance is discussed.

None of our patients suffered any ill effects from the shunts, but these might be potentially harmful during lymphography if their possible existence were not remembered or if the normal limitations on the volume of contrast material were exceeded.

Detection of Lymphovenous Shunts

Technique of Lymphography and Materials Used

The technique of lymphography was essentially that described by Kinmonth (1952), Kinmonth and Taylor (1954), and Kinmonth *et al.* (1955), where lymph trunks are made visible by preliminary subcutaneous injection of patent blue violet and and after isolation one of them has been cannulated with a needle.

In patients under investigation the contrast material used to delineate lymphatics has since 1962 been Ultrafluid Lipiodol.[1] This material is less rapidly dispersed should it enter the blood stream than the water-soluble iodine compounds which were used before 1962. It also gives much clearer delineation of the lymphatic system, particularly of the nodes. Ultrafluid Lipiodol is injected by means of an automatic injector at the rate of about 10 minutes for each millilitre. For an adult, up to 7 ml. of Ultrafluid Lipiodol for each lower limb has been injected.

The course of the infusion is followed carefully by means of radiography. Where suspicion of lymphovenous shunts appear

[1] Bengue Ltd., Mount Pleasant, Alperton, Middlesex (now marketed by May & Baker).

on the initial films, repeated radiographs are made and the infusion is stopped.

In some patients the image intensifier has been used to monitor the course of injection. Repeated observation can be made and radiographs taken.

A large group of patients received therapy to lymph nodes involved with neoplastic disease. In these patients the materials administered by direct intralymphatic injection were either ^{131}I or ^{32}P Lipiodol. Much smaller volumes are used than in investigative lymphography (Edwards, 1966; Edwards and Kinmonth, 1968). The course of the infusion to the lymph nodes is monitored carefully by the following method:

(1) Early radiography of the limb and lymph node areas after injecting 1–2 ml. of radioactive material. Repeated radiographs are taken of the lymph node areas or the image intensifier is used to study lymph node filling.

(2) External scanning with two collimated Geiger counters. One is fixed over the regional node area which is being treated while the other is used to follow progress of the radioactive material up the limb and also to scan the lung fields. A rise in counts over the lungs indicates lymphovenous connexions and consequently the injection is immediately stopped.

Radiological Criteria for Lymphovenous Shunts

The criteria that we have defined as indicating the presence of a lymphovenous shunt may be summarized as follows:

(1) The delineation of an anatomically recognizable vein. Confirmation of the actual vein involved by phlebography.

(2) A globular pattern of Ultrafluid Lipiodol which occurs occasionally when the oil contrast material enters the blood stream. The "caviare sign."

(3) Delineation of a large vessel not initially recognizable as a vein. Rapid clearance of contrast material in serial radiographs indicates that a vein has been outlined as opposed to a lymph node.

(4) Delineation of an organ—for example, liver—which cannot occur other than by the presence of a lymphovenous shunt.

Delineation of Anatomically Recognizable Veins

Case I.—A married woman aged 42 had a melanoma on the inner aspect of the left thigh over the course of the long saphenous vein. The lesion was excised down to deep fascia, the long saphenous vein being divided and a segment removed. A skin graft was placed over the defect. Six weeks later intralymphatic therapy with ^{131}I Lipiodol was given from the dorsum of the left foot. Radiographs taken during the procedure showed intense lymphatic regeneration around the grafted area and also, towards the end of the injection, dye in the long saphenous vein. The injection was stopped. An *x*-ray film taken later revealed elimination of contrast material from vein and lymphatics except for a little residuum in and around lymphatics in the grafted area (Special Plate, Fig. 1 A and B; arrows show dye in vein). There was no ill effect from the small volume of dye shunted into the blood circulation.

Identification of Vein Involved by Phlebography

One of the best methods of confirming a shunt to a vein is to demonstrate by phlebography the actual vein involved.

Case II.—A married woman aged 48 was investigated for oedema of the right lower limb. Initially, pelvic phlebography was performed which showed a normal venous pattern in the pelvis without pelvic vein obstruction. The following day bilateral pedal lymphography was done to investigate the lymphatics of the lower limbs. On the right side an obstructive lymphoedema pattern was shown with dermal lymphatic filling. On the left side, the clinically normal limb, the lymphatic pattern was hypoplastic, as is often found in lymphoedema. In the pelvic area a shadow was shown which was suspected as a vein. Following cessation of the injection a repeated radiograph five minutes later showed rapid elimination of contrast material, indicating that a vein had been filled. This on studying the previous phlebogram could be identified as the obturator vein (Special Plate, Fig. 2 A, B, and C). Other clinical features and the subsequent benign course of the malady confirmed a diagnosis of primary lymphoedema.

Globular Pattern. "Caviare" Sign

The caviare sign may be seen if Ultrafluid Lipiodol passes into the blood stream. It is due to globules which fail to coalesce and fill the vessel completely. It is only very occasionally seen in lymph vessels and only under special circumstances.

Case III.—A man aged 67 had carcinoma of the urinary bladder with involvement of iliac lymph nodes shown by lymphography. Contrast material was seen in iliac veins broken up into globules. It was dispersed in the blood stream as shown by a later radiograph (Special Plate, Fig. 3 A and B).

Studies with Image Intensifier

The image intensifier was useful to demonstrate shunts. Delineation of a large vessel not initially recognizable as a vein may occur. The rapid clearance of the contrast media, which can be seen by frequent observation, confirms that a vein has been outlined as opposed to a lymph node shadow where the contrast material remains.

Case IV.—A married woman aged 48 had a carcinoma of the left breast treated by simple mastectomy. It was followed three weeks later by infusion of the remaining left axillary node with ^{131}I Lipiodol. The course of the infusion was followed with the image intensifier. A shadow with the typical "fishtail" appearance, like that often seen in phlebography of the venous valves, appeared during the course of the infusion. This shadow was suspected as a vein, and the infusion was stopped. The vein was observed to empty, and a radiograph taken at the conclusion of the procedure confirmed this (Special Plate, Fig. 4 A and B).

Delineation of Liver due to Lymphovenous Shunting

Opacification of an organ such as the liver which would not normally fill after pedal lymphography is evidence of lymphovenous shunting.

Case V.—A man aged 41 had a seminoma of testis with gross metastatic spread to the retroperitoneal nodes. Lymphography by injection into foot lymphatics confirmed the nodal involvement, but following the procedure opacification of the liver was also noted. This must have occurred in the basis of a lymphatic-portal vein shunt (Special Plate, Fig. 5).

Results

An examination has been made of 700 lymphograms done with oil contrast media since 1962 for the presence of lymphovenous shunts. These were done for diagnosis and also in patients receiving therapy to lymph nodes involved with malignant disease.

The results are shown in two groups of patients (see Table). First are those with normal appearances on clinical and lymphographic grounds. This was a smaller group of 148 patients, comprising in the main patients with venous oedema and those receiving therapy to lymph nodes, with ^{131}I or ^{32}P Lipiodol, whose lymph nodes appeared normal on lymphogram examination. In this group no lymphovenous shunts were discovered, as assessed by the radiographic criteria already described or by scanning studies.

The larger group of patients studied were those with abnormal appearances on lymphographic studies. These

patients comprised those with primary and secondary lymphoedema and also those with various lymph node infections. These included nodes involved by metastatic tumour with obvious involvement of the nodes by alteration of the normal architecture, or else nodes involved by primary lymph node malignancy (various lymphomas). From this larger group of 552 patients 16 lymphovenous shunts were identified, an overall incidence of 2·9%. Three were found in patients with primary

Lymphovenous Shunts Observed During Lymphographies

State of Lymph System	No. of Patients	Pathology	Lymphovenous Shunts
Normal	148	Venous oedema Stage I carcinoma Stage I melanoma Miscellaneous	0
Abnormal	552	Lymphoedema	3
		Lymphoma	3
		Carcinoma of vulva	1
		Carcinoma of bladder	1
		Carcinoma of prostate	1
		Carcinoma of breast	2
		Carcinoma of rectum	1
		Seminoma	1
		Melanoma	2
		Skin graft	1

lymphoedemas, an incidence of roughly 1% in the patients with these disorders. Ten more were found in patients with lymph nodes involved with malignant disease, both primary and secondary. Some of these patients also had oedema of the limbs due to lymphatic obstruction. The incidence of lymphovenous shunts in patients with lymph node involvement was at least 5%. Two of these patients had lymphovenous shunts detected by scanning as well as by radiological methods. Both were patients with melanoma affecting the lower limb, stage II disease with obvious involvement of regional lymph nodes. One of these had been subjected to lymph node biopsy. In this patient intralymphatic therapy was attempted and ^{131}I Lipiodol given from the dorsum of the foot. The radioactive material was observed on radiographs to reach the inguinal area and also monitored by the collimated Geiger counter. At this point the scanning Geiger counter over the lung fields began to show activity. This indicated that a lymphovenous shunt must have occurred and the injection was immediately stopped.

Lymphovenous shunts were detected in three patients with Hodgkin's disease and in nine with node metastases from a variety of different primary tumours.

In this group of patients with abnormal lymph nodes there was also one patient who had a lymphovenous shunt in relation to a skin graft. Details regarding this patient have already been given.

Discussion

The first finding from this study was that lymphovenous connexions other than the thoracic duct termination were not seen in patients with lymphatic systems which had been classified as normal. Shunts were seen only from disorganized tumour-involved nodes or else in patients with lymphoedema. It must be emphasized that the true incidence of lymphovenous shunts is probably higher than that presented, as in only the therapeutic group were special efforts made to detect them. The shunts may represent normal anatomical mechanisms compensating for abnormal pressure gradients in the lymphatic system or they may merely occur on the basis of destruction of node architecture.

It seems that lymphovenous shunts may have clinical significance in three ways.

(1) In the primary lymphoedema group of patients the presence of lymphovenous connexions may protect a limb from the overt development of oedema. The shunts were sometimes found in limbs that had a definite lymphatic abnormality yet were clinically normal. An excellent example was given in one of the case presentations of a woman (Case II above) with a bilateral lower limb lymphatic defect. Only one limb was oedematous, the other had a lymphovenous shunt. Much effort is now made to produce lymphovenous shunts by surgical methods, but only certain patients appear suitable on the basis of the existing lymphatic anatomy. Such methods comprise implanting lymph nodes into veins (Nielubowicz and Olszewski, 1968) or direct implantation of lymph vessels (Kinmonth and Edwards, 1968).

(2) The significance of lymphovenous shunts in malignant disease is also of interest. This occurrence is of obvious theoretical disadvantage, as by the presence of a shunt early passage of tumour cells into the main venous circulation may occur. The exact role of the shunt with regard to the prognosis is difficult to evaluate but could be of significance.

(3) Lastly, with regard to lymphographic technique, it is obvious that the operator should be aware of the presence of lymphovenous connexions and that precautions should be taken to detect them. This is particularly so in therapeutic lymphography where radioactive materials are injected, as a theoretical hazard could occur from passage of isotope to the lungs. The precautions described as part of the technique seem efficient in detecting lymphovenous connexions. It is well to be especially on guard in patients who have gross involvement of lymph nodes by malignancy, those who have secondary lymphoedema, and those who have had previous surgical operations.

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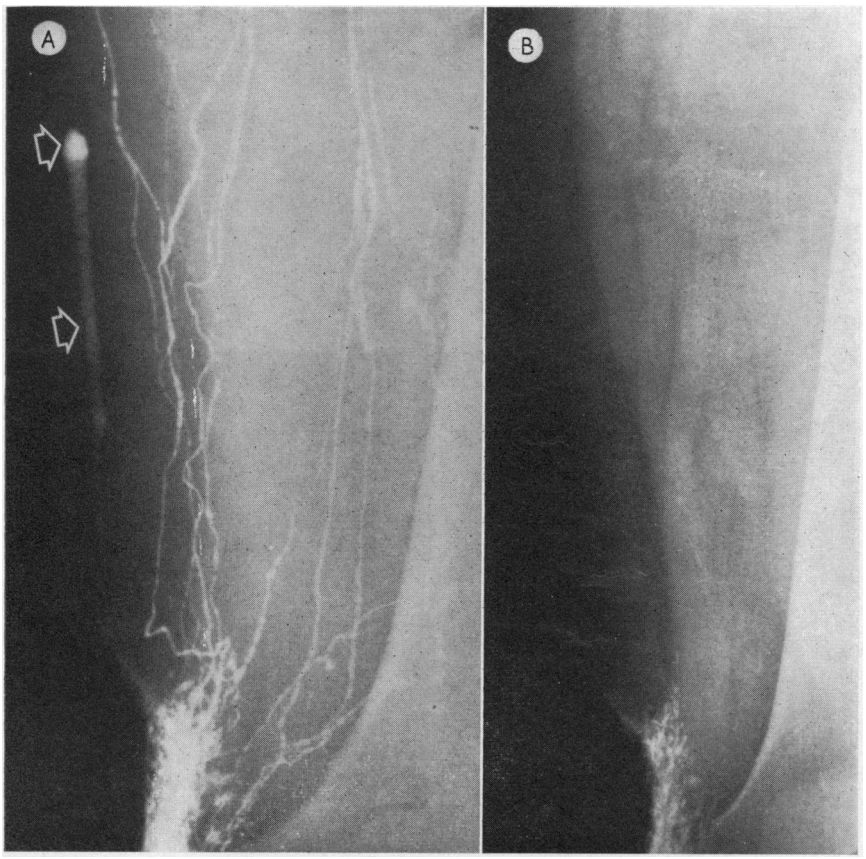

FIG. 1

FIG. 1.—Case I. (A) Arrows show dye in great saphenous vein during injection of Lipiodol into a foot lymphatic. A split-skin graft had been applied six weeks previously. Numerous lymphatics are visible near the graft region (bottom left) and normal superficial and deep lymphatics in the lower thigh. (B) Later radiograph. Dye has cleared from the vein and from most lymphatics. Further details in text.

FIG. 2.—Case II. Normal pelvic phlebography in patient with oedema of right lower limb. The vein area shown by the arrow was subsequently outlined during lymphography. (B) Lymphography shows abnormal inguinoiliac lymph pathways but also outline of part of one of the veins previously seen on phlebography (arrow). (C) Radiograph five minutes after (B). Dye has disappeared from the vein. Only abnormal lymph pathways remain visualized. (The shadow at bottom left of picture is diodone in the bladder following the previous phlebogram.) Further details in text.

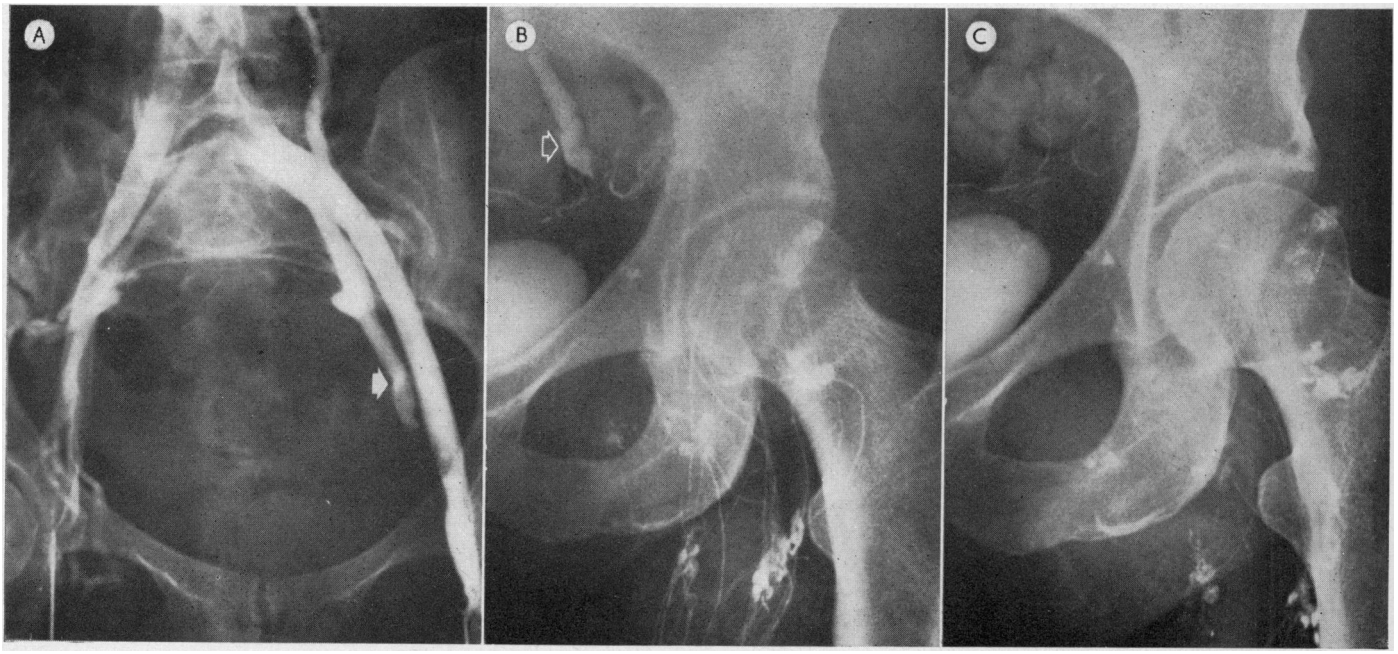

FIG. 2

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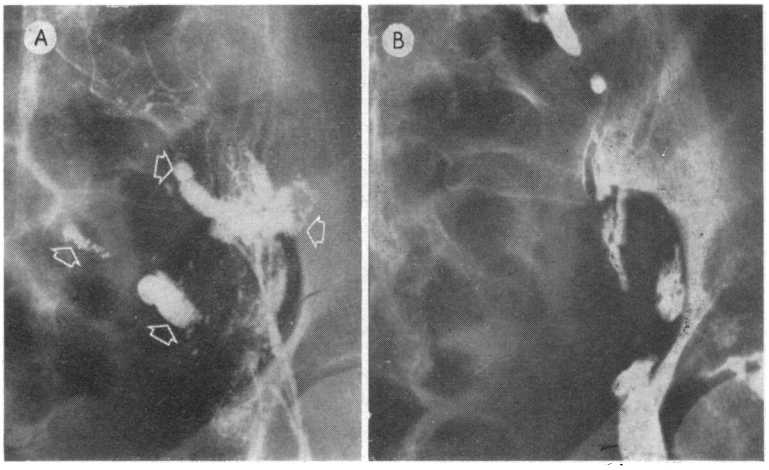

FIG. 3.—Case III. Carcinoma of bladder with pelvic lymph node involvement. (A) Globules of oil contrast medium in pelvic veins, the "caviare" sign. Arrows indicate oil in veins. (B) Taken 24 hours later, shows the Lipiodol to have left the veins and lymphatics. Outlines of dye-filled nodes only remain (lymphadenograms).

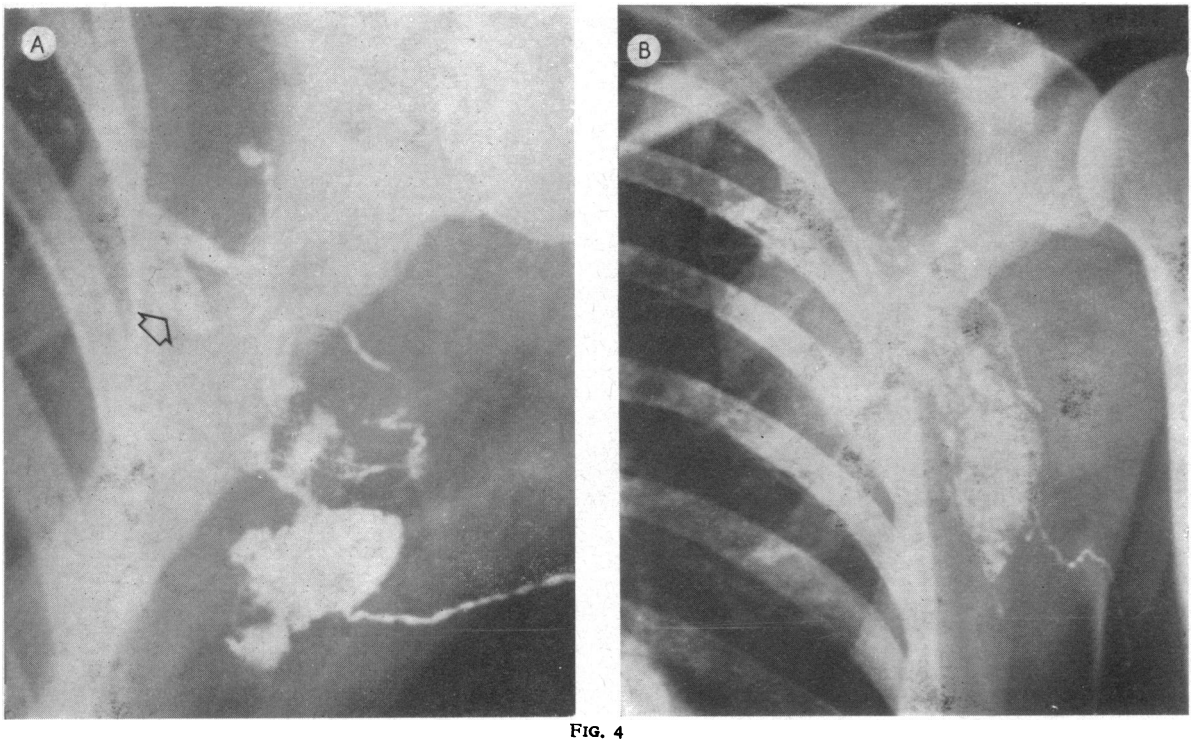

FIG. 4

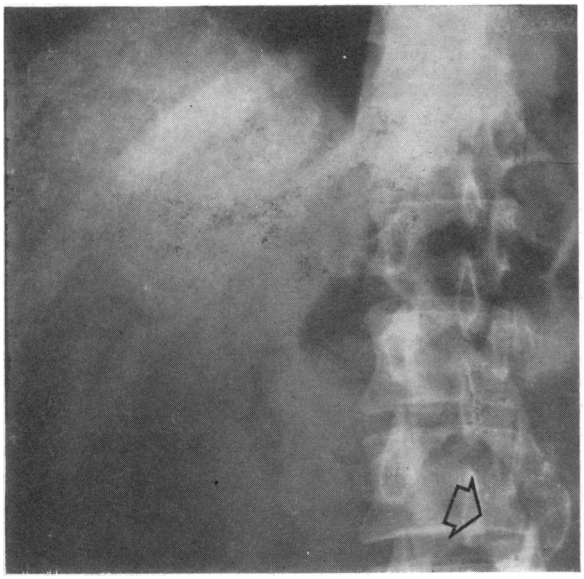

FIG. 5

FIG. 4.—Case IV. Radiographs of axilla of patient with stage III carcinoma of breast. Lipiodol injection into lymph vessel in arm shows axillary lymph vessels and also contrast medium filling part of axillary vein with the characteristic fishtail shape of a valve (arrow) in (A). The venous filling was seen under the image intensifier to be fleeting. A radiograph taken half an hour later (B) confirmed that the fishtail shadow of the vein had gone.

FIG. 5.—Case V. Opacification of vessels in liver, top left of picture, overlying lower three ribs occurred in a man who had gross involvement of retroperitoneal nodes secondary to seminoma testis. The outline of one of the involved nodes with a contrast-filling defect is seen to left of third lumbar vertebra (arrow, bottom right of picture).