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CLINICAL USE OF INDIRECT LYMPHOGRAPHY IN DIFFERENT FORMS OF LEG EDEMA

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ABSTRACT

Indirect lymphography by subepidermal infusion of newly developed non-ionic, dimeric contrast media (e.g., Iotrolan) opacifies peripheral lymphatics of the skin. Using this method we examined 159 patients with primary and secondary lymphedema, chronic venous insufficiency, and lipedema and compared the findings to normal individuals. A variety of characteristic patterns were uncovered. The technique causes little patient discomfort and takes on the average only 30 minutes.

After subepidermal infusion of suitable contrast media, indirect lymphography allows radiological demonstration of lymph collectors and, in the presence of insufficient lymphatic valves, of initial lymphatics as well in skin regions of interest. The spread of the contrast media at the injection site is also documented on radiographs.

As with various patterns of spread of patent blue (1,2), typical constellations similarly exist for indirect lymphography depending on the underlying form of edema. To pursue further the use of this "radiological blue test" we examined the value of indirect lymphography in a variety of patients with primary and secondary lymphedema, chronic venous insufficiency, and lipedema, and compared the findings to normal individuals (controls).

MATERIALS AND METHODS

The contrast media used was Iotasul initially and Iotrolan subsequently--two substances recently developed by Schering AG, Berlin. Both are water soluble, non-ionic, hexaiodinated, with particularly good local tolerance. Each is virtually isotonic with blood and cerebrospinal fluid and chemotoxicity has been sharply reduced (3).

The contrast medium is administered subepidermally at an average infusion rate of 0.12ml/min with the aid of thin butterfly needles (size 20-25) and an infusion pump. Exact subepidermal positioning of the tip of the needle is of paramount importance to facilitate a "contrast depot" from which lymphatics fill. The depot is optimal when the resulting wheal displays a bluish, glassy center.

Four subepidermal depots are usually induced simultaneously. The injections are given into skin regions with pathological changes and symmetrical contralateral sites can be used for comparison in case of unilateral abnormalities.

Filling of the lymphatics, which normally begins after a few minutes, is observed on an image converter and doc-

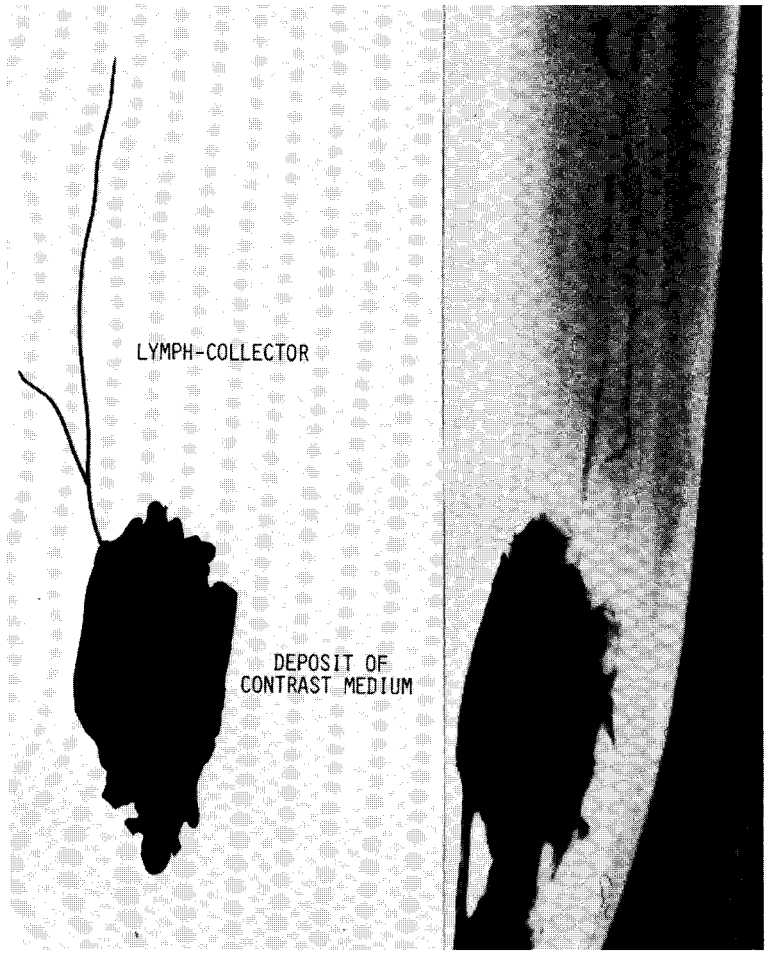

Fig. 1. Normal finding of indirect lymphography of the medial lower leg.

umented on mammography films at intervals of 5 min. 159 patients were examined including 52 with primary lymphedema, 65 with secondary lymphedema, 20 with chronic venous insufficiency, 10 with lipedema; 12 patients with normal legs acted as controls. Patient age was from 6 months to 83 years.

RESULTS

Normal legs

In the healthy lower extremity, the depot appears as an encircled structure, roundish in the vertical projection, and ellipsoid in the lateral projection. The borders may be slightly indistinct and irregular as "fronds" or "clouds". Normal lymph collectors fill from these depots *(Fig. 1)* and, when injection is into the back of the foot, can sometimes be followed to the knee. Opacification, however, is usually adequate only to just above the ankle joint. Regional lymph nodes in the popliteal space and groin are rarely demonstrated.

Primary lymphedema

The initial lymphatics and peripheral collectors show in general four patterns (4). The main characteristics are summarized in *Table 1*.

Table 1
Lymphatic Patterns in Primary Lymphedema

	Type I Milroy's Bilateral Congenital Lymphedema	Type II Lymphedema Precox and Tardum Distal Forms (Mild)	Type III Lymphedema Precox and Tardum Distal and Proximal Forms (Severe)	Type IV Chronic Lymphedema Lymphedema Tardum
Initial Lymphatics	-	+	+	-
Peripheral Collectors	+	-	+	-
Incidence	7/52	30/52	9/52	6/52

Type I (n=30). Only a roundish or ellipsoid depot is demonstrated without filling of lymphatics. The contrast medium may sometimes diffuse along a vascular sheath *(Fig. 2)*.

Type II (n=30). The contrast medium depot is a roundish or ellipsoid structure from which extremely fine initial lymphatic networks are filled. Fine collectors become visible after a slight delay *(Fig. 3)*. The peripheral collectors appear attenuated.

Type III (n=9). There is notable filling of initial networks which join tortuous, hyperplastic lymph collectors *(Fig. 4)*.

Type IV (n=6). Characterized by a complete lack of demonstrable lymph vessels. In most cases, the consistency of involved skin is dense and thick.

Secondary lymphedema

With proximal obstruction of lymph flow (e.g., lymph nodal metastases), initial lymphatics and peripheral collectors are dilated and increased in number--as in Type III primary lymphedema.

Chronic venous insufficiency

The contrast medium depot is an encircled structure from which irregularly shaped and sometimes fragmented lymphatics are filled. Translucent zones occur nearby as contrast medium extravasates and retrograde filling of initial lymphatics (dermal backflow) occurs in dermatosclerotic areas. The collectors display a wide caliber, and under an image converter have increased contractility *(Fig. 5)*.

Lipedema

Lateral films show that the contrast medium depots are flame-shaped instead of encircled and ellipsoid. The individual tongue-like projections taper and end in normal-appearing lymph collectors. In the vertical projection, the depots display a loose, honeycomb-like structure *(Fig. 6)*.

Side effects

Spontaneous, reversible local erythema occurred in 5 patients after injection of contrast and erysipelas developed in one instance. One other patient had a systemic allergic reaction with urticaria which disappeared after corticoid therapy.

DISCUSSION

Direct lymphography with oily contrast material for verification of the diagnosis of lymphedema has generally been abandoned. Its use is restricted for

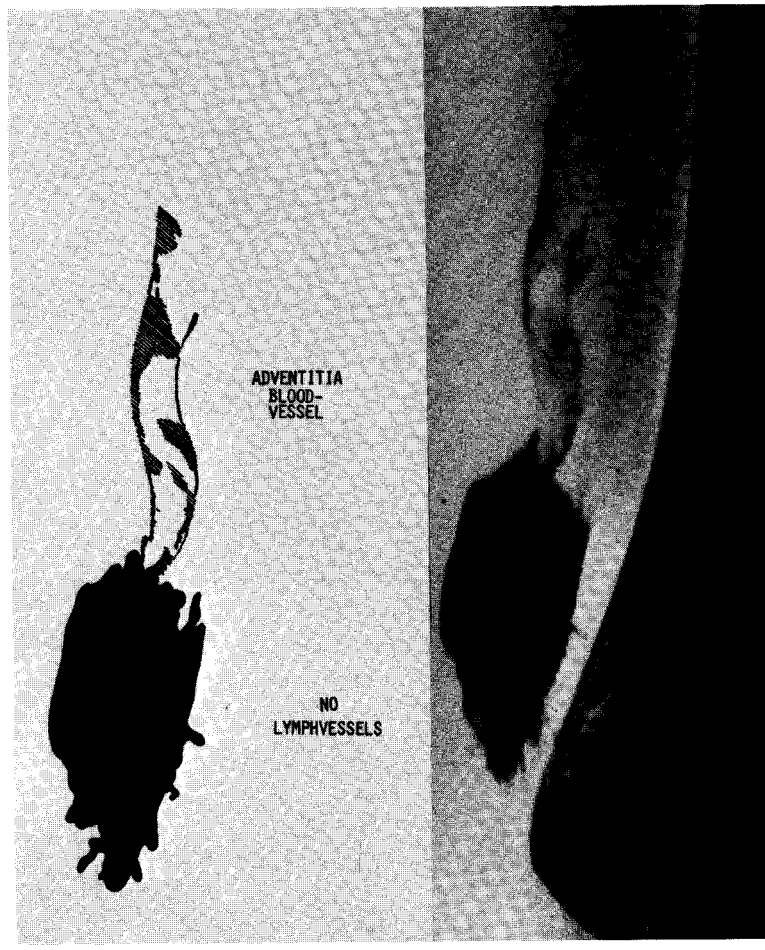

Fig. 2. Indirect lymphography in primary lymphedema ("type I") at the medial lower leg. No lymphatics are seen as the contrast medium spreads in a proximal direction along the adventitia of a blood vessel.

lymph node visualization with suspected neoplasia after examination by ultrasound and computerized tomography (5). The value of direct lymphography with water soluble contrast media for routine diagnosis is also questionable.

A highly useful and virtually non-invasive method of confirming the diagnosis of lymphedema is isotope lymphography with its various modifications (6,7). However, these procedures yield more functional than morphological information. The availability of new contrast media which, because of their excellent tissue tolerance, can also be administered intracutaneously, makes indirect lymphography possible (3). In animal species (8) other than man, lymph collectors as well as regional lymph nodes are opacified using this method. In humans, however, visualization of regional lymph nodes is rare, probably because water soluble contrast media, as in direct lymphography, is overly diluted with lymph in the large collectors. Despite this limitation, indirect lymphography is useful for the diagnosis of lymphedema with little discomfort to the patient. The main advantage lies in assessment of contrast material into the adjacent tissue and lymphatic system, and as the present study shows, the various forms of edema dis-

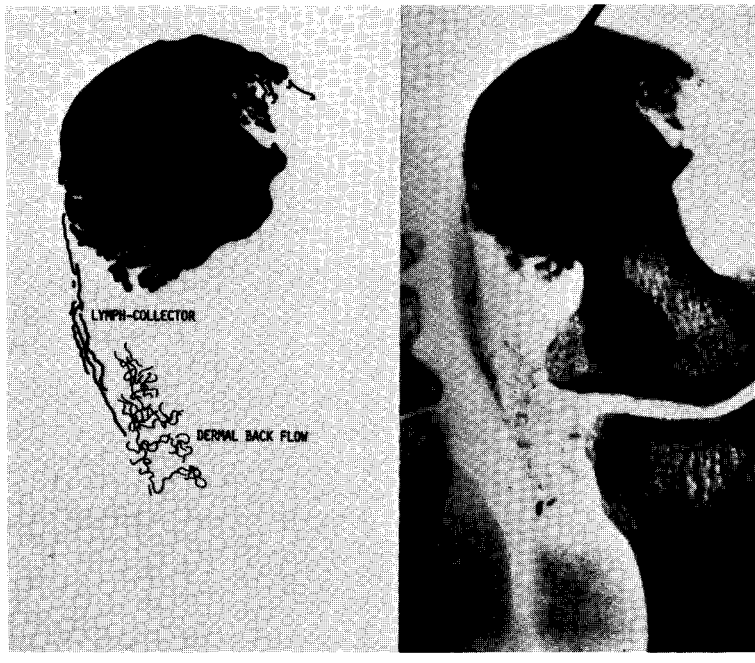

Fig. 3. Indirect lymphography in primary lymphedema ("type II") of the big toe. Collectors run in a proximal direction from the depot and a pathologic network of lymphatics fills at the level of the interarticular space (dermal backflow).

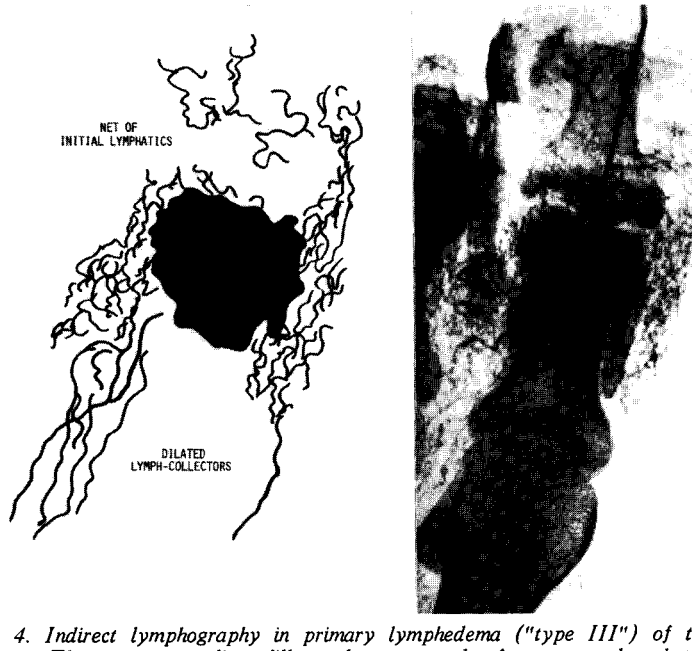

Fig. 4. Indirect lymphography in primary lymphedema ("type III") of the big toe. The contrast medium fills a dense network of cutaneous lymphatics of relatively large caliber from which several dilated and tortuous lymph collectors emerge.

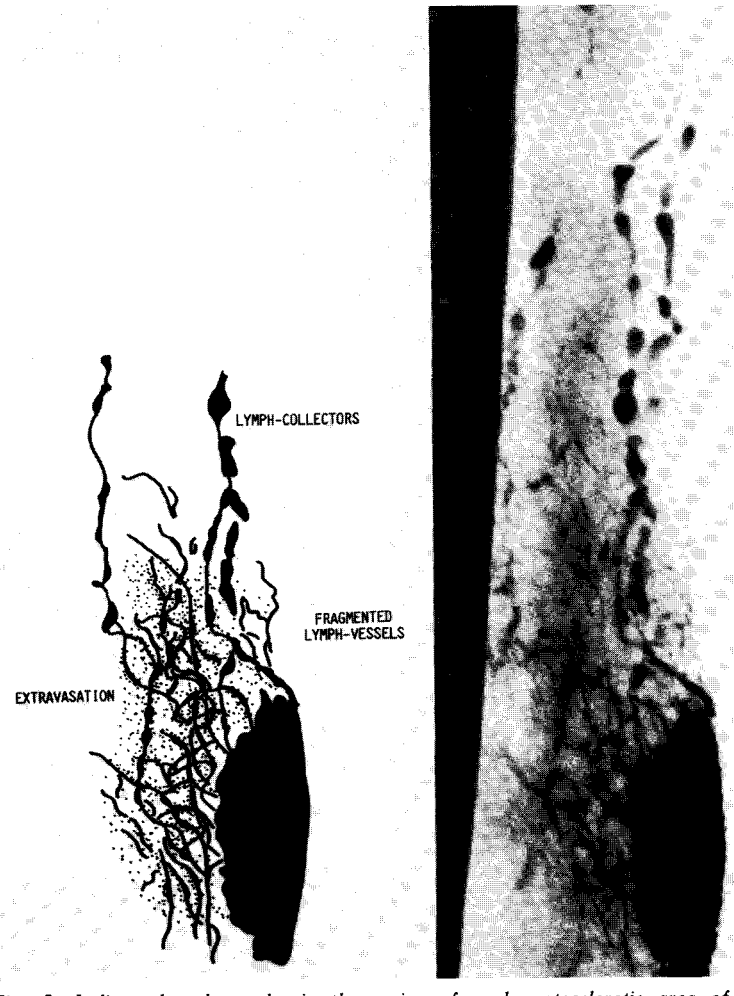

Fig. 5. Indirect lymphography in the region of a dermatosclerotic area of the medial lower leg in chronic venous insufficiency. Collectors of strikingly large caliber with distinct segmentation (valves) are seen with diffuse opacification in the region of the peripheral lymphatic network as contrast medium extravasates.

play characteristic patterns of contrast medium diffusion.

Normally there is a roundish, encircled contrast medium depot which communicates directly with fine lymph collectors via minute spurs. Initial lymphatic networks are not visualized. Probably because of progressive dilution of water soluble contrast material, only the distal segments of the collectors can be adequately assessed. Lymph nodes are not usually seen. Earlier we demonstrated normal collectors of human fingers and toes by this method and observed the course of regeneration of lymphatic following reimplantation of free flaps (9).

Mainly collectors of the ventromedial bundle are demonstrated after injection into the interdigital folds and the back of the foot, whereas depots in the region of the outer malleolus and heel fill lymphatics of the dorsolateral bundle. The tip of the infusion needle must be located in the dermis to visualize lymphatics. Lymphatic pathways are not seen after a subcutaneous or intramuscular instillation. Accordingly, the method is not suitable for demonstration of subfascial

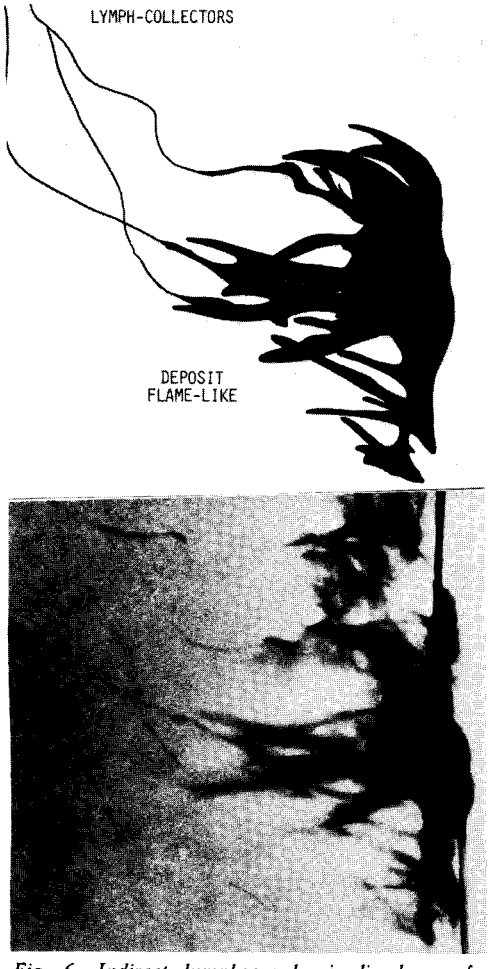

Fig. 6. Indirect lymphography in lipedema of the medial lower leg. Flame-shaped contrast medium depots communicate directly with normal collectors.

lymphatics.

In lymphedema, indirect lymphography regularly reveals pathological and characteristic findings. It is now possible to document a form of lymphedema characterized by at least partial aplasia of initial cutaneous lymphatics despite even hyperplastic lymph collectors ("type I")(4,10). Using microlymphangiography, Bollinger and co-workers obtained similar results in regard to the initial lymphatics, but they were unable to assess the peripheral lymph collectors (11,12). This group of patients with usually congenital and sometimes hereditary forms of lymphedema is of special clinical importance. On the one hand, these patients have previously been classified as "aplasia" on the basis of absent lymphatics on direct lymphography. On the other hand, operations such as lymph-venous shunts or autologous lymphatic transplants in the region of the root of the extremity are pointless in such patients because the peripheral initial lymphatic segments are lacking.

Mild forms of lymphedema in young women (lymphedema precox) but also peripheral swellings which do not become manifest until after the age of 35 years and remain confined to the foot and ankle (lymphedema tardum, distal form), are sometimes so subtle that an additional, confirmatory diagnostic test is desirable. It is precisely in these patients where highly characteristic abnormalities are seen on indirect lymphography, with retrograde filling of fine lymphatic networks (dermal backflow) occurring via incompetent lymphatic valves. This finding has been confirmed by microlymphangiography (12). The large collectors appear to be attenuated ("type II") in keeping with the findings of direct lymphography, which places these patients into the group of "hypoplasias" (13).

Patients with "type III" primary lymphedema display pronounced swelling in the region of the lower leg and thigh. This group includes both patients with congenital and acquired lymphedema. The retrograde demonstration of cutaneous lymphatics and tortuous hyperplastic collectors seemingly corresponds to the constellation of "proximal hypoplasia with distal distension" (13). The primary lesion is presumably situated in the proximal lymph nodes. It is not surprising that, in secondary lymphedema, there are analogous lymphographic findings since the site of obstructed lymph flow is also proximal.

In 6 patients with lymphedema tardum we were unable to demonstrate lymphatics, and this constellation has been termed "type IV". The skin was uniformly thick and hard. It is still unclear whether dermatosclerosis made

lymphatic demonstration impossible for technical reasons or whether "die back" occurred from a fusion of the lymphatics (14).

Lymphographic studies in chronic venous insufficiency has added greatly to our knowledge of the pathogenesis of the skin changes in this disorder (15). As a result of longstanding venous hypertension there is increased tissue extravasation of fluid and to a lesser extent large protein molecules, and the lymphatic load increases (16). This process can be observed in the distended collectors, which display increased contractile activity under the image converter and which can often be followed as far as inguinal lymph nodes. With excess work placed on lymphatic transport, functional insufficiency ultimately develops and as a result, the extravasated protein is less efficiently cleared. In addition, increasingly severe changes occur in the lymphatics within the dermatosclerotic areas: they fill only irregularly, are less well defined, and display progressive changes in caliber. The contrast medium accordingly readily extravasates into the tissue network and retrograde filling of fine channels occurs as a result of progressive valvular incompetence. Using microlymphangiography, Bollinger and co-workers made analogous observations in the region of the lymphatic capillaries (17).

Lipedema is a swelling of the leg in which there is a tendency for fluid to accumulate in the fatty layers. The tendency for edema to form has been explained by an increased influx of fluid due to a low intersitial pressure within the fatty tissue in the presence of orthostasis (18). Instead of an encircled, round depot, indirect lymphography reveals typical flame-shaped contrast medium depots from which in some female patients, drainage takes place into normal-appearing collectors. The "tongues of flame" likely represent extremely distended prelymphatic spaces which are filled by the injection pressure in the presence of low tissue resistance. The pattern of spread of the contrast medium probably corresponds to the connective tissue fibers which criss-cross around the lobules of fat and which function as "low resistance pathways" (19). The collectors fail to opacify in other women as the injection pressure leads only to distension of the prelymphatic spaces (20). The morphology as demonstrated by indirect lymphography corresponds to the pathogenetic concept of lipedema advanced by Földi (21). Similar patterns can be found in areas of skin with an extremely thick subcutis (e.g., in the fatty tissue apron of the abdomen) where tissue resistance is probably also low.

In conclusion, indirect lymphography with newly developed dimeric contrast media is useful for delineating the pathogenesis and diagnosis of a variety of peripheral edemas.

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