Lymphography—Clinical and Experimental

Brendon W. M. Gooneratne

Butterworths

Lymphography — Clinical and Experimental

EDITED BY

BRENDON W. M. GOONERATNE

MBBS (Ceylon), DAPE (London), PhD (London)

Department of Diagnostic Radiology,
The Prince Henry Hospital, Sydney;
formerly Beit Memorial Medical Research Fellow,
London and Senior Lecturer, Faculty of Medicine
Peradeniya, Ceylon

BUTTERWORTHS

ENGLAND: BUTTERWORTH & CO. (PUBLISHERS) LTD.
LONDON: 88 Kingsway, WC2B 6AB

AUSTRALIA: BUTTERWORTHS PTY. LTD.
SYDNEY: 586 Pacific Highway, 2067
MELBOURNE: 343 Little Collins Street, 3000
BRISBANE: 240 Queen Street, 4000

CANADA: BUTTERWORTH & CO. (CANADA) LTD.
TORONTO: 14 Curity Avenue, 374

NEW ZEALAND: BUTTERWORTHS OF NEW ZEALAND LTD.
WELLINGTON: 26–28 Waring Taylor Street, 1

SOUTH AFRICA: BUTTERWORTH & CO. (SOUTH AFRICA) (PTY.) LTD.
DURBAN: 152–154 Gale Street

Suggested U.D.C. Number: 616·42–073·7

ISBN: 0 407 26140 0

Printed in Great Britain by William Clowes & Sons Limited
London, Beccles and Colchester

Lymphography —

Clinical and Experimental

for

Yasmine

Contributors

J. IAN BURN, FRCS
Consultant Surgeon, Charing Cross Hospital, London; formerly Senior Lecturer, Royal Postgraduate Medical School and Consultant Surgeon, Hammersmith Hospital, London

KEVIN M. CAHILL, MD, DTM & H (Lond)
Professor of Tropical Medicine, The Royal College of Surgeons in Ireland; Director, The Tropical Disease Center, New York City

J. S. CALNAN, FRCP, FRCS
Professor of Plastic and Reconstructive Surgery, University of London, at the Royal Postgraduate Medical School and Hammersmith Hospital, London

OSCAR CRAIG, FRCSI, FFR
Consultant Radiologist, St. Mary's Hospital and Bolingbroke Hospital, London; Director of Clinical Studies, St. Mary's Hospital Medical School, London; Teacher in Radiology, London University; Lecturer in Radiological Anatomy, King's College, University of London

BRENDON W. M. GOONERATNE, MBBS (Ceylon), DAPE (Lond) PhD (Lond)
Department of Diagnostic Radiology, The Prince Henry Hospital, Sydney; formerly Beit Memorial Medical Research Fellow, London and Senior Lecturer, Faculty of Medicine, Peradeniya, Ceylon.

PETER G. HERMAN, MD
Associate Professor of Radiology, Harvard Medical School, Boston

J. J. PFLUG, MD, PhD
Honorary Lecturer and Tutor in Surgery, Royal Postgraduate Medical School and Hammersmith Hospital, London

S. B. SEN, MB (Cal), FRCS (Eng)
Assistant Professor of Surgery, Jawaharlal Institute of Postgraduate Medical Education and Research, Pondicherry

Preface

For quite a time now there has been a pressing need for a comprehensive and up-to-date book on the various aspects of human and animal lymphography. In our present age of specialization in which comparatively new methodology rapidly becomes part of routine clinical investigation (for instance in the field of cancer diagnosis, prognosis and therapy), the valuable contribution that lymphography can make to medical knowledge is now widely recognized. There is no doubt that lymphography will in the future become increasingly important in experimental studies of all kinds, and open a path to new knowledge of the lymphatic system, anatomy, physiology and pathology of the animal kingdom.

A scanning of the literature indicated at an early stage in the preparation of this book that its greatest usefulness would be to the surgeon, the radiologist, the basic research worker, the lymphologist and the postgraduate student. With this audience in mind, experts in their respective fields of study were invited to contribute chapters to it. To my co-authors, therefore, who received my suggestions with enthusiasm; who despite arduous clinical, teaching, research and administrative duties completed their chapter-contributions to an editorial deadline; and whose experience and skills have shaped my own contribution, I owe particular debts of gratitude and this book its comprehensiveness.

Illustrations have been selected with a view to providing a vivid pictorial record of the text. Particular care has been paid to the provision of clear and accurate photographs and diagrams, since visual representations of good quality are of paramount importance in understanding radiology. Each chapter has an abbreviated bibliography to facilitate quick reference, while a general detailed bibliography will be found at the end of the book. In the chapter on Lymphography in Experimental Filariasis I would like to emphasize that a detailed account not normally given in books of this nature has been included, in order to illustrate the widening scope of lymphography, and especially its increasing value in experimental studies on the lymphatic system.

I would like to take this opportunity of acknowledging my debt to my teachers and colleagues, and to the many authors and research workers whose contributions in the field have guided me in the preparation of this book. I am particularly grateful to Dr. G. H. du Boulay of the Nuffield Institute of Comparative Medicine, who by his encouragement and co-operation helped my continuing interest in lymphography to see fruition. He and Dr. M. N. Jilla, Consultant Radiologist of the Ceylon Army Hospital extended a warm and deeply appreciated welcome to me, and I am especially obliged to them both for arranging for my use of the radiological facilities in their busy departments.

To Miss Evelyn Monson, Professor G. S. Nelson, Dr. L. G. Goodwin, Mrs. Pamela du Boulay and Dr. J. S. Macdonald I am very grateful indeed for co-operation and advice

without which the initial lymphographic research that resulted in the planning of this book would not have been possible. To my wife Yasmine, whose continuous encouragement showed itself in patient help during the book's minor setbacks and pleasure in its successes; to the secretarial assistance of Mrs. N. M. P. Hettiaratchi; to Mr. J. G. Mahawatte's photographic skill; and to Miss Wimalasuriya's willing co-operation in the preparation of some of the diagrams, I owe debts that it gives me pleasure to acknowledge.

Finally, I would like to mention my appreciation of my publishers' imagination and enterprise.

Brendon W. M. Gooneratne

Contents

1 *Introduction*

BRENDON W. M. GOONERATNE

HISTORICAL

Although the Greeks as early as 300 BC and subsequently the Alexandrian school, were aware of the existence of the lymphatic system it was not until Gaspar Aselli discovered the mesenteric lacteals of a well-fed dog in 1627 and Ludwig collected lymph from various parts of the body that systematic examination of lymph and the lymphatic system in man and animals began. Ludwig was the first to state that lymph was a filtrate of the blood. This hypothesis was conclusively proved by Starling after many years of bitter controversy.

Following on this, Pecquet (1651) described the cisterna chyli and thoracic duct in a dog and subsequently chyle vessels in man. These observations awoke a new interest in mapping out the anatomy and investigating the functional physiology of the colourless thin-walled lymphatics and the well-defined group of nodes. The efforts of Thomas Bartholinus (who coined the term 'vasa lymphatica' for the lymphatic vessels) and Olaf Rudbeck, the brilliant Swede who first demonstrated the existence of valves in the system and the joining of the thoracic duct with the great veins in the mediastinum, shine as outstanding contributions to our present knowledge of the lymphatic system. Rudbeck also postulated that blockage of the lymphatics produces ascites and oedema.

In 1692 Nuck employed the technique of intralymphatic injection of mercury to outline the lymphatic system. He is said to have demarcated the human lymphatic system employing this method. Mascagni (1784), Cruickshank (1798) and Gerota (1896) devised modifications of this technique which enabled Barthels (1909) and Jossifow (1904–30) to conduct comprehensive topographical studies of the human lymphatic system.

The first recorded experiments in visual lymphography were reported by Braithwaite (1923) and by Hudack and McMaster (1933). The former injected the dye indigo carmine into the paracaecal region to investigate lymph flow in living cats, while Hudack and McMaster investigated the minute lymphatics of the human skin after intradermal injection of a diffusible dye (Patent Blue V) dissolved in a small quantity of fluid. This enabled observations to be made on the diffusion of dye in the connective tissue, its absorption by the skin lymphatics and its appearance in the lymphatic system distant to the area of injection.

With the discovery of x-rays in 1895 and their increasing application in investigating and

treating human disease from the 1920s, research workers have attempted to utilize them to obtain further knowledge of the anatomy and physiology of the lymphatic system. Various radio-opaque media were injected subcutaneously and into the serous cavities. In 1931 Carvalho, Rodriques and Pereira injected Thorotrast intranodally in order to visualize the efferent lymph vessels on x-ray. Pfahler (1932) injected Lipiodol into the maxillary sinuses and demonstrated the distribution of the lymph drainage which had extended upwards and downwards, and as high as the zygoma. Menville and Ane (1932) also injected Thorotrast intrapleurally into animals to outline the diaphragmatic and thoracic lymphatics.

Of the various radio-opaque media used in human work, Thorotrast briefly dominated the stage by virtue of its important property of selective absorption by the subcutaneous lymphatics. However, with the gradual realization of its radioactive and carcinogenic properties, and because of its slow excretion from the body, the use of Thorotrast declined in human work. This proved a costly setback, as the interest generated in the radiological investigation of the lymphatic system and its diseases lessened as a result, until 1952 when Kinmonth used larger quantities of Patent Blue dye than were first employed at the Rockefeller Institute by Hudack and McMaster in 1933, to delineate the lymph trunks and nodes in clinical investigation of the lymphatics. By 1954, Kinmonth *et al.* had perfected the technique of direct visual limb lymphography. This valuable contribution opened up a new field of clinical and experimental investigation of the lymphatics and lymph nodes. With the introduction of newer and better oily contrast media that cause fewer side effects and achieve clearer delineation of the lymphatic trunks and nodes the technique of lymphography has provided the clinician, radiologist, surgeon and research worker with an extremely valuable tool for the study and investigation of the lymphatic system and its abnormalities and diseases.

2 *Lymphographic Procedure*

BRENDON W. M. GOONERATNE

MATERIALS

In order to perform routine lymphography a sterile trolley containing the following equipment is necessary.

(1) 2 ml syringes with 19 or 21 swg needles and drawing-up needles for Patent Blue V dye.

(2) 2 ml syringes and needles to draw up and inject local anaesthetic (2 per cent lignocaine hydrochloride or procaine hydrochloride with adrenaline).

(3) Sterile normal saline.

(4) Skin disinfectant—spirits.

(5) A scalpel with blades.

(6) 3–6 curved arterial clamp forceps.

(7) 1 toothed forceps.

(8) 1 large and 1 fine dissecting forceps.

(9) 4 towel clips.

(10) Disposable gamma-sterilized St. Thomas's Hospital type lymphangiogram sets; *or*

(11) 36 in long polyethylene tubing with a 30 swg needle and a 20 ml Luer–Lok syringe at the other end; *or*

(12) An alternate improvized cannula.

(13) Surgical needles with holder.

(14) Silk 000 and nylon sutures.

(15) Sterile towels.

(16) Sterile gauze swabs.

(17) Spring clips 1–2 cm long and 0·4–0·6 mm wide with rubber bungs at the tips to clip needle in the lymphatic.

Before the instruments are sterilized, they should be cleaned with ether.

Angle-poise or other adjustable lamp with a bright bulb.

PREPARED MATERIALS

The following prepared materials are necessary for lymphography.

(1) 2 per cent Patent Blue V either in ampoules (commercially available in 2 ml ampoules), or as a solution prepared from the powder and autoclaved in Bijou bottles or ampouled and sterilized.

(2) 2 per cent procaine hydrochloride or lignocaine hydrochloride, with adrenaline 1/100,000—local anaesthetic.
(3) Lipiodol Ultra-Fluid (*see page* 7) 10 ml or 15 ml ampoules.
(4) Pethidine hydrochloride 75 mg ampoules for premedication (or barbiturates).
(5) Antibiotic dressing.

Instead of the disposal set devised by Kinmonth and now commercially available as the St. Thomas's Hospital type lymphangiogram set, cannulae have been prepared for use by heating a length of polythene tubing to a fine point. Polyethylene tubing is superior, however, in that it is more flexible and does not kink when wound around or twisted round the toes on cannulation.

INJECTORS

Electrical motor-driven injectors (*Figure 2.1*) or mechanical weight-driven injectors (*Figure 2.2*) are both quite suitable for lymphography. Previous calibration of the rate of flow of contrast medium is necessary, especially with the weight-driven apparatus.

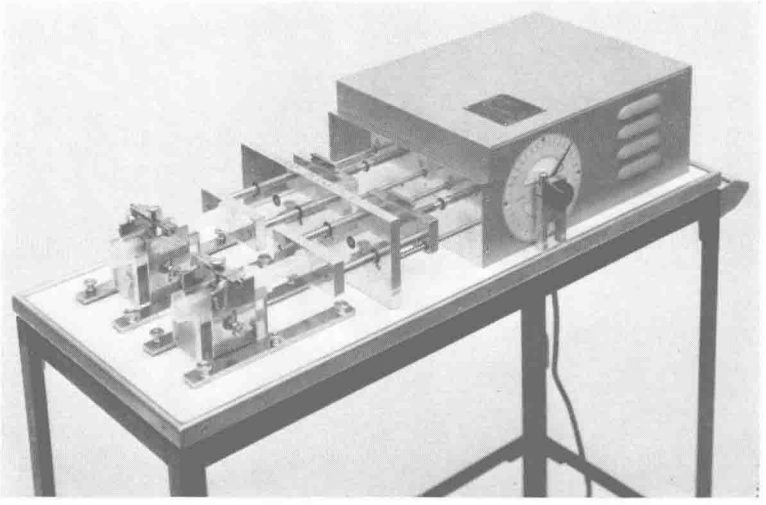


Figure 2.1. An electrical motor-driven apparatus for lymphography. (Reproduced by courtesy of Dr. Oscar Craig)

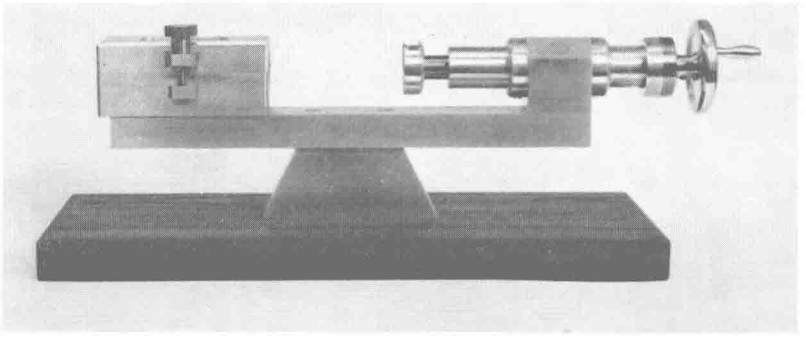
PROCEDURE

The technique is first explained to the patient, whose written consent is then obtained for the investigation. The patient is also informed of the temporary bluish colouration of the skin and urine resulting from the Patent Blue V. Premedication with pethidine hydrochloride (50–75 mg intramuscularly) has given excellent results. With infants or with young children general anaesthesia is advisable.

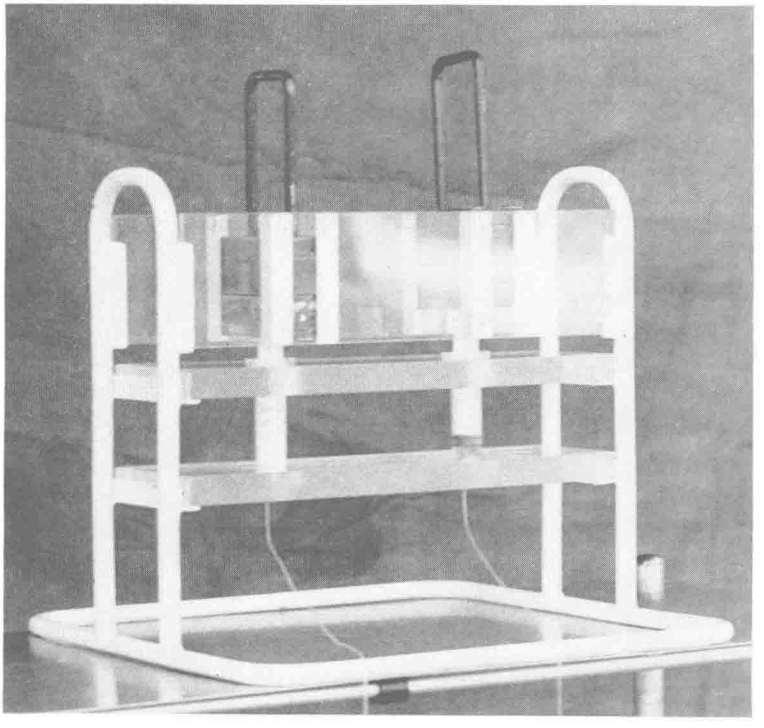
In limb lymphography the patient should lie flat on the x-ray table or on a comfortable stretcher with a pillow under the knees and foam-rubber rests under the heels. Once cannulation has been effected, the patient must be made aware of the importance of keeping the cannulated limb still while the contrast medium is being injected.

The skin of the area receiving the incision is swabbed with spirits and the spirits allowed

to dry. The adjacent area is draped with sterile towels. In selecting the line of incision an area on the same horizontal plane as the needle is chosen to enable the needle to lie flat on the dorsum of the foot. Lignocaine with adrenaline 1–2 ml (into two adjoining sites) is



(a)



(b)

Figure 2.2. Mechanical weight-driven injectors for lymphography. ((a) Reproduced from Cahill 1965 by courtesy of the author and Editor, J. trop. med. Hyg.*)*

injected subcutaneously over the selected incision site, followed by 2 ml Patent Blue V dye, into the webs of the toes/fingers in divided doses. The limb is then massaged for a few minutes, and the patient is asked to flex and extend the extremity to facilitate lymph and

thereby dye flow. In lymphoedematous patients these active movements are necessary to outline any available lymph channels. It is preferable to wait for about 10 minutes after the injection of the blue dye to enable the lymphatics to selectively absorb it.

A superficial transverse incision 2–3 cm long and confined to the dermis is made over the selected area 6 cm proximal to the web spaces, and the wound swabbed until the field is bloodless (*see Figure* 10.1). This is particularly important in filarial patients with lymphoedema where bleeding is more profuse than normal. An incision made too distally would have the twin disadvantages of (a) being in the blue-coloured region caused by the Patent Blue V dye, and (b) encountering a network of finer lymphatics which are more difficult to cannulate. Some clinicians employ a longitudinal incision over the first metatarsal or second metacarpal space about 3–4 cm long, midway between the phalanges and the ankle or wrist joints. However, in lymphoedematous patients, a transverse incision is more desirable. The subcutaneous tissue is then carefully dissected until a greenish-blue vessel is visible (*Plate 1*). This lymphatic vessel is then cleared of fascia for about 1–2 cm, the proximal area pressed down with the left forefinger while the distal area is milked upwards to distend the lymphatic. Previous to this a length of silk 2–4 cm is passed underneath the lymphatic chosen for cannulation in order to steady the vessel when the needle is pushed into it. The lymphatic is lifted up by this loop of silk held in the left hand, and the right hand pushes the needle into the lumen of the vessel. When cannulation has been effected the tip of the needle would be seen inside the bluish vessel and gentle pressure of the piston of the syringe containing the contrast medium will confirm this when the onward flow of Lipiodol Ultra-Fluid now makes the lymphatic appear colourless by pushing the blue dye onwards. In order to steady the needle inside the lumen of the lymphatic, the loop of silk may be tied round the vessel over the needle, but a loop round the appropriate toes/fingers before cannulation also steadies it. A metal spring-clip with rubber-bunged tips keeps the needle in place.

The wound is kept continually moist with sterile normal saline, and occasional flooding with saline would help in detecting any leakage of contrast medium or dislodgement of the needle, in which event oily droplets would be seen floating on the saline. The contrast medium is allowed to run for about 1·5–2 hours at a rate of flow of 3–4 ml/hour, with a maximum of 7 ml per lower limb and 4 ml per upper limb for an average sized male. The literature enclosed with the commercially marketed contrast medium should be consulted before use, and the instructions set out there carefully adhered to.

Sometimes a fresh lymphatic has to be cannulated while at other times the vessel could be cannulated more proximally if the fascia covering the lymphatic vessel were cleared fairly extensively at the beginning. In either case a further 0·5 ml of blue dye when injected into the corresponding web space just before recannulation helps in locating and distending the lymphatic.

When the injection of contrast medium is completed the needle is gently withdrawn, the silk loop removed and the wound cleaned with disinfectant. One ml of local anaesthetic is injected before suturing commences if there is local pain. This is not usually necessary as local anaesthesia of the region persists. An antibiotic dressing is used, especially in lymphoedematous patients, and the wound is closed with several sutures depending on the length of the incision. A dry gauze dressing is used and a crepe bandage wrapped loosely to allow for overnight swelling of the limb. The patient is advised to take two tablets of calcium aspirin or other mild analgesic when he gets home and to return for wound dressing in 3 days. The sutures are removed in 7–10 days when follow-up x-rays are taken. Follow-

up x-rays in 24 hours are desirable, and this often necessitates hospitalization. Measurements are taken of the distances between the cassette and the width of the area through which the x-ray travels, and the focus distance.

Films are exposed after 1 hour and after 3 hours. Films are again exposed after 24 hours, and in cases of contrast medium retention, also after 1 week.

CONTRAST MEDIA

Patent Blue V

Patent Blue V (a visual contrast medium) is a dye, the chemical structure of which is given in *Figure 2.3*. It is a diamino compound of a triphenylmethane dye and is officially termed Acid Blue 3 and labelled number 42051 in the Colour Index published by the Society of Dyers and Colourists and the American Association of Textile Chemists and Colorists.

Patent Blue V is selectively absorbed by the lymphatics and excreted in the urine. It also colours the blood serum blue. It colours the site of injection for about 2 weeks in pale-skinned patients who should be warned of this possible reaction. In some countries a sensitivity test is performed with 0·02 ml before subcutaneous injection of the normal dose.

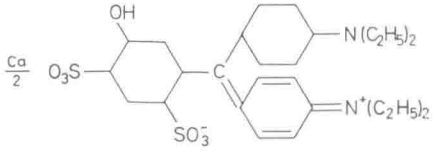


Figure 2.3. Chemical structure of Patent Blue V

Lipiodol Ultra-Fluid (Ethiodol)*

Lipiodol Ultra-Fluid (Ethiodol) is an iodized poppy seed oil containing glyceryl esters of oleic, linoleic, linolenic, palmatic and stearic acids. It contains 37 per cent of iodine, is yellowish in colour, and viscous. It is stable when stored sealed, away from the light. Heat and air contact causes decomposition of the oil with iodine liberation, producing a dark brownish colour. This is a contraindication to its usage.

Fischer and Zimmermann (1959) and Koehler, Wohl and Schaffer (1964) have evaluated the oil experimentally in animals. In man the contrast medium, when injected in the prescribed dosage, is found in the nodes and lesser amounts in the lungs. Nodes opacify for varying periods, even up to 1 year, while the concentration in the lungs is greatest at 2–3 days after lymphography. The contrast medium is removed via the circulation and also by the macrophages. In addition it is excreted in the kidneys after conversion into an inorganic form.

REFERENCES

Cahill, K. (1965) *J. trop. Med. Hyg.* **68**, 27
Fischer, H. W. and Zimmermann, G. R. (1959) *Am. J. Roentg.* **81**, 517
Koehler, P. R., Wohl, G. T. and Schaffer, B. (1964) *Am. J. Roentg.* **91**, 1216

* Marketed by E. Fougera and Co., Hicksville, New York, USA as Ethiodol, and by Laboratories Andre Guerbet, Paris, France and by May and Baker, Dagenham, England under the name of Lipiodol Ultra-Fluid.

3 *Applications and Importance of Lymphography*

BRENDON W. M. GOONERATNE

INTRODUCTION

Lymphography is an established x-ray technique in most radiological units and has proved invaluable in the investigation of human disease, both primary and secondary, involving the lymphatic system. It has been increasingly employed since Kinmonth perfected the direct injection technique in 1952 and the subsequent discovery of the advantages of oily contrast media outlining the lymphatic vessels and nodes. A practical drawback has been, however, the time-consuming procedure it necessitates. Also, it is occasionally difficult to actually cannulate a lymphatic vessel. Sometimes in grossly oedematous limbs it is practically impossible to isolate a lymphatic vessel for injection. These limiting factors occur only on rare occasions but this has been a minor restricting factor in its usefulness as a diagnostic investigation technique. Wilder (1964) stated that 'Aortography was 20 years old before it received popular acceptance' and that lymphography has accelerated basic studies of the lymphatic system, 'the last great body system to be so explored'.

Direct visual lymphography with oily contrast media has so far provided the best results. Apart from its application in human work, its usage in experimental studies in animal work has commanded new frontiers in the understanding and knowledge of the dynamics of lymph flow in the lymphatic system. Animal experimental models have provided us with the basis for investigating specific disease processes and evaluating the actions and uses of intralymphatic drug therapy. Recent work in both man and animals strongly suggests that the dynamics of lymph flow and efficient lymph carriage is related intimately to the presence of collateral lymphatics, often dormant, and the presence and efficiency of lymphovenous communications. Aspects of this new thinking and the vital role played in its elucidation by lymphography will be discussed in Chapters 5, 6, 7 and 8. Wallace *et al.* (1964) suggested that the presence of lymphovenous shunts, both demonstrable large communications in the presence of lymphatic obstruction and also cellular level small shunts not visualized by lymphography, played a vital role in the manifestation of lymphatic derangement. Burn's work (1968) using radioisotopes has confirmed this.

The difficulty of experimentally inducing lymphoedema in animals has so far been a drawback in conducting research work on experimental physiology and pathology of acute and chronic lymphoedema. Man is the only known animal which manifests lymphoedema, though a localized lymphoedematous condition is said to occur around the