# Complications of Lymphography

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In 1954 Kinmonth first described lymphography as a radiological method of studying the lymphatic system in living human subjects. Kinmonth used a water-soluble contrast medium (diodone) which was non-toxic and produced good visualization of the lower-limb lymphatics. However, it suffered from the drawback that it rapidly diffused out of the lymph vessels and failed to show the ilio-pelvic lymphatics satisfactorily. Hreshchyshyn and Sheehan (1960) described the use of an oily medium, Ethiodol (known as Lipiodol Ultra Fluid in Europe). Because it did not diffuse into the tissues it was possible to visualize the retroperitoneal lymphatics and even the thoracic duct. Furthermore, as some of the contrast medium was retained in the lymph nodes for many weeks, they found the technique useful for assessing the extent of retroperitoneal node disease and could measure the effects of treatment procedures on node size. Since then lymphography has often been used as a diagnostic and therapeutic aid in the management of malignant disease affecting the lymphatic system (Wallace *et al.*, 1961 ; Schaffer *et al.*, 1963 ; Viamonte *et al.*, 1963 ; Chiappa *et al.*, 1964).

Because lymphography may become more widely used it is important to consider the complications associated with the procedure.

## Present Study

One hundred and fifteen consecutive female patients with a carcinoma arising from the genital tract were studied, and any complications which developed were carefully recorded. In 98 a bilateral lymphographic study was made ; in 12 the study was unilateral, and in five it was not possible to inject a lymph vessel on either side. The carcinoma was confined to the primary site in 29 patients. This was confirmed by histological examination of excised lymph nodes and by careful palpation at operation. Forty-six patients were studied after lymphadenectomy, and in another 21 the carcinoma had already spread to involve the lymphatics. In the remaining cases it could not be determined with certainty whether or not the lymphatic system was involved by metastases.

A repeat lymphographic study was made in 20 patients ; in eight this was bilateral and in 12 unilateral. The time interval separating the two studies varied between one day and 15 months.

The technique used has already been described (Jackson, 1966). A lymph vessel on the dorsum of the foot was isolated and between 6 and 8 ml. of Lipiodol Ultra Fluid was injected intralymphatically. The total amount injected in any patient did not exceed 16 ml. The rate of injection was never greater than 1 ml. in 10 minutes, and the time taken for the procedure was three to four hours.

## Complications

Twenty-five patients had an elevation of pulse rate or temperature over a period of 24–72 hours. Three of these had associated shivering attacks, and another three complained of generalized aches and pains. Nine patients complained of nausea, and five vomited on one or two occasions. Delayed healing or infection of the incision of the dorsum of the foot occurred in 10 patients ; seven of these received local treatment, and three required systemic antibiotic therapy.

One patient developed oedema of a whole lower limb on the evening of injection, and this occurred in another patient three days after injection. A diagnosis of deep venous thrombosis was made in both cases. Another patient developed classical signs of pulmonary thrombo-embolism on the fifth day, and on the next day oedema appeared in both lower limbs. These three patients had extensive malignant disease in the pelvis.

Six patients complained of an irritating productive cough with streaks of blood in the sputum over a period of five to 12 days. In one patient this developed two days after injection ; in two patients three days after injection ; in another two patients four days after injection ; and in the sixth patient eight days after injection. None of these complained of any other symptoms. On clinical examination the chest was clear, and no lower-limb oedema or calf tenderness was present. On chest *x*-ray examination 24 hours after injection definite evidence of pulmonary oil embolization was seen in two patients, and minimal signs were present in the others. In four cases the lymphographic study was made after pelvic lymphadenectomy, in one case the ilio-pelvic nodes were metastatically involved, and in the remaining case no abnormality of the lymphatic system was detected. The total amount of Lipiodol Ultra Fluid injected varied between 7.5 and 13.5 ml. (average 12.2 ml.).

## Discussion

The complications described in the literature have usually been of a minor nature. The only serious complication reported has resulted from pulmonary oil embolization. Four deaths have been recorded which were attributed to this cause (Desprez-Curely *et al.*, 1962 ; Koehler *et al.*, 1964 ; Fraimow *et al.*, 1965 ; Howett and Elmendorf, 1965). Evidence of oil embolization may be seen on chest *x*-ray examination in many cases (Gough *et al.*, 1964), but the development of untoward effects depends on the amount of contrast medium which directly reaches the lungs and on the presence of pre-existing pulmonary disease.

Guiney *et al.* (1964) investigated the toxicity of Lipiodol Ultra Fluid in rabbits. They injected intralymphatically a dose in excess of 0.6 ml./kg. on 13 occasions, and nine rabbits died towards the end of the injection or within two hours of completion. The cause of death in each case was massive pulmonary embolization of Lipiodol Ultra Fluid. On nine occasions when they injected a dose less than 0.6 ml./kg. there were no deaths. They recommended that the maximum dose to be used for clinical purposes should never exceed 0.25 ml./kg. body weight. Bron *et al.* (1963) advised caution when studying patients with lymphatic obstruction. They found a higher incidence of pulmonary embolization on chest *x*-ray examination in these circumstances, and suggested that the opening up of lymphatico-venous anastomoses might have allowed more oil than usual to reach the lungs.

Fraimow *et al.* (1965), studying the changes in pulmonary function after lymphography, found that the diffusion capacity

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of carbon monoxide was consistently reduced, though no patient complained of increased dyspnoea, cough, haemoptysis, or chest pain. They obtained lung biopsy specimens from patients undergoing thoracotomy, some of whom had had lymphography performed on the day of operation and others on the day before. Histological examination revealed that oil emboli initially cause pulmonary capillary obstruction, and that in the next 24 hours there is considerable clearing of oil from the capillary bed into the interstitial tissues and then into the alveoli. This deposition in the interstitial tissues of the lung causes interference with gaseous exchange between alveoli and capillaries. Three of the four recorded deaths following a lymphographic study occurred in patients who had pre-existing pulmonary disease, producing an alveolar-capillary block syndrome.

## Present Series

The minor complications which developed have been described by most other workers, but there has been little previous reference to two complications, thrombo-embolism and haemoptysis, encountered in the present series.

The development of deep venous thrombosis and thrombo-embolism may have been coincidental. The association between this complication and extensive malignant disease is well known, but venous stasis occurring during the course of the investigation was probably a contributory factor. (Over a period of three to four hours the limbs had been completely immobile and were resting on a firm mattress.) Since these occurrences a soft foam-rubber mattress has been used, and while the injection was continuing the limbs have periodically been passively exercised.

There are very few reports of haemoptysis occurring after lymphography. Litwin *et al.* (1964) described the case of a patient who developed a temperature of 105° F. (40.6° C.), dyspnoea, cyanosis, and mild haemoptysis following the investigation. They did not specify the time interval between injection and the development of these symptoms, but remarked that they responded rapidly to cortisone therapy. Gough *et al.* (1964) described the case of a patient who developed calf pain and haemoptysis 12 days after a lymphographic study; they assumed that this patient had a pulmonary infarct.

It is surprising that haemoptysis occurring some days after injection and unaccompanied by other symptoms had not been mentioned by other workers when describing the complications of lymphography. Many of the studies, however, were done on patients who were discharged after 24 hours. When they returned to have sutures removed from their feet they may not have been seen by the person directly interested in lymphography.

Hamilton *et al.* (1964) showed that pulmonary fat embolism can be divided into two phases: a mechanical phase, and a chemical phase in which fatty acids released by hydrolysis of the fat (or oil) damage the capillaries and alveolar cells. In cats killed half an hour after intravenous injection of triolein or mineral oil the appearances in the lungs were essentially normal, but in those killed four days after injection they found areas of haemorrhagic consolidation in which the alveoli were filled with blood and exudate. Similar haemorrhagic changes in the lungs were found in cats killed half an hour after the injection of oleic acid. These findings suggest that the haemoptysis which occurred in the six patients described in the present study resulted from a breakdown of oil and release of fatty acids in the lungs. Schaffer *et al.* (1963) found in necropsy studies that only very minute quantities of Lipiodol Ultra Fluid got into the general circulation, and that most of that which was not retained by lymph nodes was removed in the lungs.

Tjernberg (1962), investigating the properties of various contrast media in lymphography, considered that oily media were unsuitable for clinical use. He believed that they caused permanent damage to lymph nodes. In the present study 20 patients had a repeat lymphographic investigation. Evidence that temporary obstruction develops was found when an injection was made in one patient on two successive days. On the second occasion, despite using much pressure, the contrast medium would not pass the most inferior inguinal nodes, and extravasation occurred from the lymph vessels along the whole length of the limb. However, in all other patients, restudied within 4 to 15 months, no alteration in the pattern of lymph flow or in the appearance of opacified nodes was seen that could be attributed to the previous investigation. Other workers (Jackson *et al.*, 1961; Viamonte *et al.*, 1963) have made repeat studies without observing any changes in the lymphographic appearances.

Sections from lymph nodes excised between 18 hours and nine weeks after injection were stained with haematoxylin and eosin and examined histologically. An intense foreign-body reaction to the contained oil was seen in those excised between four days and two weeks after injection (Fig. 1). The reaction then appeared to regress, and nine weeks after injection there was an obvious reduction in the number of oil spaces usually seen. Many of those present no longer had a distinct outline, and appeared to be partially collapsed (Fig. 2). On radiographs these nodes had a more granular appearance than is seen 24 hours after injection, suggesting that only the larger oil globules were still present. Usually, six months after injection only faint opacification of nodes can be seen. Thus the contained oil seems to be slowly removed from the lymph nodes, and apart from an initial obstruction to flow no interference with the internodal or intranodal lymph circulation develops.

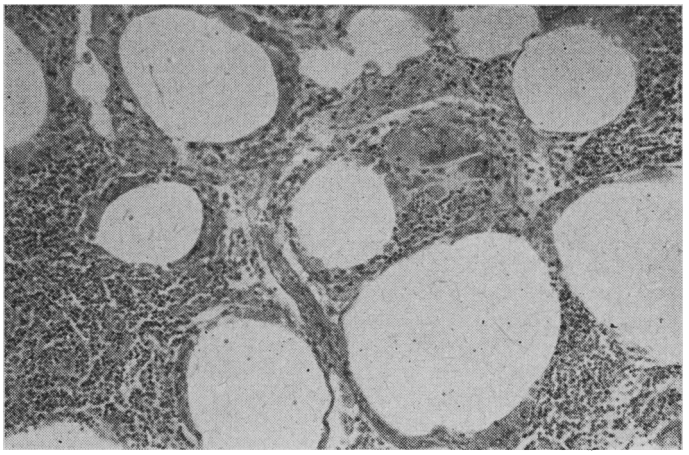

FIG. 1.—Histological section from a lymph node excised eight days after the injection of Lipiodol Ultra Fluid. Stained with haematoxylin and eosin (×60). Oil spaces lined by giant cells are closely and evenly distributed.

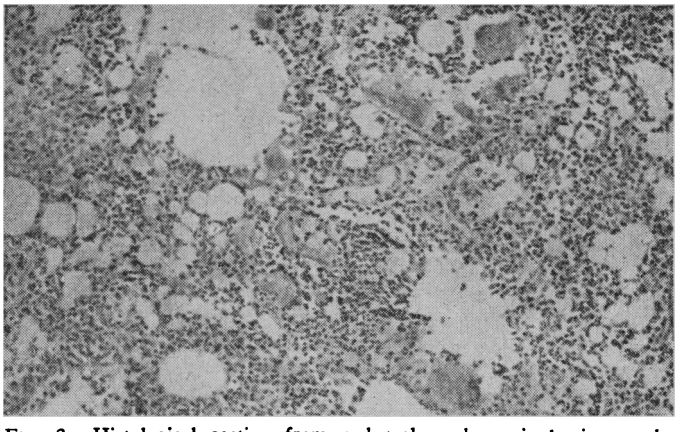

FIG. 2.—Histological section from a lymph node excised nine weeks after the injection of Lipiodol Ultra Fluid. Stained with haematoxylin and eosin (×60). The oil spaces present no longer have a distinct outline and are partially collapsed.

### Practical Considerations

From available evidence lymphography must be considered to be a potentially dangerous method of investigation. However, if certain precautions are taken no serious complications should develop. Particular care should be taken over the amount of Lipiodol Ultra Fluid injected, especially after lymphadenectomy or in the presence of lymphatic obstruction, and the procedure should not be undertaken when there is pre-existing pulmonary disease. To prevent the occurrence of thrombo-embolism it is suggested that the limbs should rest on a soft mattress, and should periodically be passively exercised while the investigation is proceeding.

### Summary

Lymphography with Lipiodol Ultra Fluid was successfully performed in 110 out of a consecutive series of 115 female patients with a carcinoma arising from the genital tract. The complications associated with the procedure were recorded. In 98 the study was bilateral and in 12 unilateral. The investigation was repeated in 20 patients; in eight this was bilateral and in 12 unilateral. The total amount of contrast medium injected in any patient did not exceed 16 ml.

Minor complications, which have been described by most other workers, developed in 30% of cases, but there has been little previous reference to two complications which occurred—thrombo-embolism and haemoptysis. The occurrence of thrombo-embolism in three patients may have been precipitated by venous stasis resulting from complete immobility of the limbs over a period of three to four hours. Haemoptysis which occurred in six patients probably resulted from breakdown of oil and release of fatty acids in the lungs.

The repeat studies indicated that no permanent interference with the internodal or intranodal lymph circulation develops after lymphography.

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# Diverticulitis: a Follow-up of 100 Cases

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In a review of acute diverticulitis McLaren (1957) observed: "This review has revealed two surprising features in the British and American literature on perforated diverticulitis. The first is the lack of adequate statistical information regarding the incidence and mortality of this condition; the second, that there has not been any investigation of the factors determining death or survival." Surgical literature does not lack expressions of opinion on the treatment of the condition, but statistical support for opinions expressed is much less in evidence.

In the search for more reliable information on the late results of treatment in diverticulitis of the colon 100 consecutive cases operated on at the West Middlesex Hospital during 1948–57 were followed up and their subsequent progress was studied. The follow-up was conducted by questionaries to general practitioners and patients, and, where necessary, by interview. Except in nine cases, the follow-up covered a minimum period of five years or until death, the maximum period being 15 years. To eliminate clinical and radiological errors the study was confined to cases in which the diagnosis had been established at operation. In all cases subject to resection the specimen has been examined histologically to confirm the diagnosis of diverticular disease of the colon, and no cases with associated pathology, such as Crohn's disease, ulcerative colitis, or carcinoma, have been included. The first operative procedure occurring in 1948–57 was regarded as the starting-point of the study, being referred to as the "definitive attack." The cases were consecutive and unselected, but exclusion of those treated non-operatively probably produced a bias towards the more severe forms of the disease. Ages ranged from the fourth to the ninth decade, females predominated by more than 2 to 1, and in all cases the disease was most severe in the sigmoid colon. The manner of presentation is given in Table I.

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