Tumor Res. 1(1966) 261-288

THORACIC DUCT CANNULATION

- An Early Diagnostic Method for Lung Cancer -

Juro Wada, Koji Ikeda, Shigeo Sugii,
and Teiko Kamiyama

Department of Cardio-Thoracic Surgery
Sapporo Medical College and Hospital

Introduction

It is common knowledge that the lymphatic system plays some role in the physiological and pathological conditions, particularly in the proliferation and metastasis of malignancy. This, however, has not been worked out in detail in Japan either clinically or experimentally because of the anatomical and histological specificity of the system. In recent years, the development of vascular surgery has made peripheral lymphangiography available for diagnosis, and has received some attention, and some papers are available on the subject (1-6).

We have reported on our clinical attempts with thoracic duct cannulation which was found useful for the diagnosis and treatment of the thoracic and abdominal diseases. The procedure involves

retrograde cannulation with polyethylene tubing into the thoracic duct at the angulus venosus for the sampling of lymph fluid. Thus the circulatory and lymphatic system can be divided and the blood and lymph can be observed independently with regard to physiological function and influence of malignancy. In the present papers, we have described the procedure of thoracic duct cannulation and reported the clinical evidences on the subject.

Indication

The importance of thoracic duct cannulation may be seen in its value as a diagnostic means, its therapeutic significance and as a research tool.

1. Diagnostic Indication

a. Exfoliative cytology in thoracic duct lymph: The value of thoracic duct cannulation has been demonstrated in various studies (7-13), in malignant tumor patients by investigating the presence of tumor cells in the blood stream and by tracking the hemogenous transport of tumor cells in an attempt to determine the relationship with the prognosis of the patient. Considerable results in the cell count rate seem to add to the diagnostic significance of this method. In the present paper, it based on the fact that patients with cancerous involvement of the regional lymph nodes show a higher incidence of tumor cells in the blood stream. The possibility was

investigated that part of the tumor cells in the blood stream may have been released from the thoracic duct lymph via the angulus venosus. With an examination on the tumor cells in diagnostic thoracic duct lymph, tumor cells in the blood stream were investigated. Together with investigation on hemogenous transport of tumor cells, the course of lymphatic metastasis was made. These studies are still under way.

b. Retrograde thoracic ductgraphy: When lymph duct contrast media is introduced via the cannulation, in malignant tumor patients, mediastinal infiltrations together with pathological changes in the vicinity of the thoracic duct are contrasted and such changes, as obstruction or distortion may be seen by giving data for the outlining of lesions development. However, the lymphangiographic contrast of metastatic lymph nodes is difficult at present time and will require further studies.

c. Simultaneous performance of Daniel's scalene node biopsy: In the presence of intrathoracic malignant tumor, Daniel's prescalene node biopsy (14) with adjacent lymph nodes in scalene fat have become a routine diagnostic means. A simultaneous introduction of thoracic duct cannulation via the same incision makes the diagnosis increasingly accurate with histological findings.

2. From the Therapeutic Point of View

a. Blockage of lymphatic extension: The ligation of the pul-

monary veins prior to other procedures at the resection of lung cancer is a routine preliminary procedure to block metastasis via the blood stream. Among cases in which thoracic duct cannulation was done, they showed no cancer cells in the preoperative lymph flow, however, they revealed an appearance of cancer cells in the lymph during operation.

It was noted that the thoracic duct lymph flow via the cannulation showed an increase immediately after the ligation of the pulmonary veins. So the thoracic lymph drainage during the operation might have a prophylactic value against the metastasis. Based on the above consideration, this method was adopted in our clinic.

b. Measurement of lymphatic concentration of anticancerous agents (In an attempt to determine the effect of the agent): The significance of chemotherapy in neoplastic diseases lies not only in the direct effect of the agent toward main lesions but also in the expectation of the blockage of metastasis at the lymph node. Thus the determination of lymphatic concentration of the agent using thoracic duct cannulation may lead to the effective administration of such agent.

c. As an investigational means for the studies of anticancerous agents: Based on the above mentioned point of view, we are considering the following three modes of anticancerous agent administration for lung cancer. The methods under consideration are general administration, retrograde thoracic duct cannulation administration and

aerosol administration with an expectation to block the malignant involvements in regional nodes.

3. Cannulation as a Means for Research

a. Studies on body fluid, lymphatic and circulatory system: Thoracic duct cannulation is used as a means in the investigation of body fluid balance, the mechanism of edema, the absorption of nutritional substances by the lymph fluid, its transportation, the factors influencing the lymph flow and studies on the lymphatic and circulatory system. Some studies using cannulation on the changes in tissue fluid during extracorporeal circulation have also been reported by others.

b. Cannulation as a means in physiological and biochemical studies of lymph fluid: Thoracic duct cannulation is utilized in studies on the changes in lymph composition in various pathologic and physiologic conditions.

c. Evaluation of lymph drainage and network in the thoracic area: In the operation of pulmonary malignancy, the limit or extent of lymph node removal is an important problem. Moreover the exact site of the lesion and information on the involved lymph nodes and drainage are the type of information needed by the surgeon. Rouvière (22) reported that the right lymphatic duct drains the lymph fluid from all parts of the intrathoracic area except a part of the left upper lobe. This has been generally accepted.

We conducted bilateral thoracic duct cannulation and collected lymph fluid from both ducts. During thoracotomy a small amount of patent blue was infused into the lung parenchyma. Then the mode of regional lymph drainage has been investigated.

d. Effect of thoracic duct lymph drainage on immune response: According to Tunner (52) et al. in skin graft operations when lymph drainage is conducted by thoracic duct cannulation, antibody production against the primary antigen is inhibited bringing about favorable results in the graft.

e. As a treatment of liver cirrhosis: When lymph drainage is conducted by thoracic duct cannulation such symptoms as portal hypertention and others show a definite improvement.

f. Intestinal absorption of lymph: Since the lymph flow through the left thoracic duct comes largely from the intestine and liver and inasmuch as part of ingested fat is absorbed by the intestinal wall and is transported into the lymph flow, thoracic duct cannulation renders the study of the lymphatic picture in various pathological conditions possible.

g. Studies on the lymphatico-venous shunt: It has been reported that in the normal living bodies where the thoracic duct opens into the vein at the angulus venosus, 98% of the total body lymph is drained into the venous system (23, 24). It has also been reported that ligation of the bilateral thoracic ducts brings about an activation of the function of the lymphatico-venous shunt. The

authors are making a follow-up by the introduction of lymphatic duct contrast media (25). As mentioned above thoracic duct cannulation is being applied widely as a means for various studies (Table 1).

Table 1. Indications for Thoracic Duct Cannulation

a. Diagnostic Indications

1. Investigations on tumor cells in thoracic duct lymph (Lung cancer, esophagus cancer, stomach cancer, and other malignant neoplasms)
2. Retrograde thoracic duct, lymphduct angiography
3. Simultaneous Daniel's biopsy

b. Therapeutic Indications

1. Prevention of metastasis during operation
2. Measurement of lymphatic concentration of agents in chemotherapy
3. Studies on local administration of anticancerous agents in lung cancer
4. Prevention of immune reaction (by drainage of lymph)

c. Research Indications

1. Studies on body fluid and lymph composition
2. Physiological and biochemical studies on lymph composition
3. Studies on intrathoracic lymph drainage
4. Intestinal absorption research
5. Studies on the lymphatico-venous shunt

A Survey of the Literature

Morphological studies on the thoracic duct were made by Moist (1908) (26), Davis (1915) (27) and Rouvière (1928) (22). However, until the advent of the vinyl tube or polyethylene tube, studies on extracorporeal thoracic duct lymph drainage and functional studies on samples thereof were impossible. Moreover, clinical studies on the thoracic duct were made based on the possibility that this duct may be a route of infection for pulmonary tuberculosis (26) or as a possible method for the surgical treatment of chylothorax (28-32). It was only in recent years that its clinical importance in malignant tumors was recognized.

The history of thoracic duct cannulation begins with Blalock's work (33) on the thoracic duct lymphatic flow in the presence of trauma and burns. In 1947, Cain et al. (34) reported the connection with liver lymph flow in dogs. This was followed by reports by Glenn (1949) (35), Slaughter et al. (1955) (36) and Linder et al. (1958) (37). In 1959, Shafirof et al. (38) succeeded in human thoracic duct cannulation. Since then various applications have been made. Based on Rouvière's report (22) that the right lymphatic duct drains the majority of lymph from intrathoracic area, Falor et al. (1962) (39, 40) emphasized the importance of bilateral thoracic duct cannulation as a diagnostic means of malignant tumor in the intrathoracic area.

In 1959, Watne (41) reported the presence of malignant tumor cells in the thoracic duct lymph while Foss et al. (42) made a similar report. Schafiroff (1959) (38) and Flemming et al. (1963) (43) reported retrograde lymph angiography. In addition numerous physiological and biochemical studies have been made on the composition of lymph fluid (44-47).

Anatomy of the Thoracic Duct

It is well known that the lymph fluid of the entire body passes through the thoracic duct and empties into the venous system through the angulus venosus on the left side of neck, however it seems to be not so well known that a separate lymphatic chain exists on the right side as the right thoracic duct through which passes the thoracic lymph flow and which is drained through a corresponding site on the right side. The thoracic duct begins in the cisterna chyli, passes upwards between the aorta and the azygos with a slight convexity to the left, and traverses behind the esophagus to the left at the level of the third thoracic vertebra where it passes upwards along the longus colli. Then at the level of the seventh cervical vertebra, it arches downwards anteriorly and terminates at the junction of the left subclavian and internal jugular veins on the anterior surface of the anterior oblique and the phrenic nerve, after receiving the three tributaries, the left jugular trunk, the left sub-

cvalvian trunk and the left broncho-mediastinal trunk. The exposure of the thoracic duct should be made at the confluence of the two veins beneath the posterior surface of the sterno-cleido-mastoid. The size of the ducts at this portion are from 3 to 7 mm in diameter. However, when the lymph flow is scarce there is a reduction in size.

The right thoracic main duct is in a corresponding site on the right, and empties into the right angulus venosus after receiving the three tributaries, the right jugular trunk, the right subclavian trunk and the right broncho-mediastinal trunk (Fig. 1).

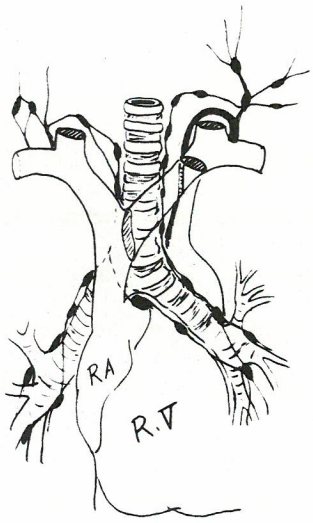

Fig.1. Lymphatic chain of chest cavity.

However, it is noted generally that the right thoracic duct has a smaller diameter and that the opening site into the vein varies.

The junction of both right and left thoracic ducts with the veins shows a considerable variation of site, and the position of junction may be classified as follows; 1. the root of the internal jugular vein, 2. the root of the subclavian vein, 3. the angulus venosus, and 4. the innominate vein. As may be seen in Fig. 2 the frequency of incidence is as shown. In most cases the junction with the vein consists of a single thoracic duct trunk. However, at times multiple channels are seen especially on the right side. In the presence of such multiple junctions, cannulation frequently fails.

Operative Procedure of Thoracic Duct Cannulation

An oral administration of 200 ml of milk or 100 grams of cream 1 to 2 hours prior to the operation, fills the thoracic duct with a miklish white fluid which also causes the duct to increase in size facilitating the location of the duct and insertion of the tube.

The patient is placed on the operation table slanted upwards with a thin pillow under the shoulders and is given a 90 degree rotation of the head to expose the supraclavicular fossa. The patient is given standard preanesthetic medication prior to local anesthesia. An incision approximately 3 to 4 cm in length is made parallel to and 1.5 cm above the clavicla, starting from the sternal fiber of the

sternocleidomastoid and extending onward beyond the lateral border of the muscle. Dissection between the platysma and midcervical fascia and the sternocleidomastoid along the axis of its two fibers exposes the deep cervical fascia. This is incised obliquely exposing the scalene fat pad, lymph nodes and internal jugular vein. Next lateral retraction of the fat pad and the omohyoid located above it is done and blunt ablation is conducted along the internal jugular towards the angulus venosus. This exposes the thoracic duct which passes behind the internal jugular and joins the vein at the angulus venosus. During the aforesaid ablation, the small lymph ducts connected with the main ducts are severed and ligated to prevent lymph leakage. Otherwise the cannulation may fail. In order to have a complete ablation and exposure of the thoracic duct at times it becomes necessary to laterally retract the internal jugular vein. Next a thin silk thread is used to ligate the thoracic duct at the root of the thoracic branch. 5 to 6 minutes later the thoracic duct swells to 2 to 3 times in its normal size. A silk thread for security is passed through the peripheral side and the polyethylene tube is inserted. Generally, because the duct wall is weak and thin, thoracic duct cannulation is difficult. In our clinic a large vein needle with a diameter to accomodate the polyethylene tube is used as a guide with satisfactory results (Figs. 4 and 5).

As for the polyethylene tube for thoracic duct cannulation a #15 tube (Fig. 6) normally used in venopuncture was found to be

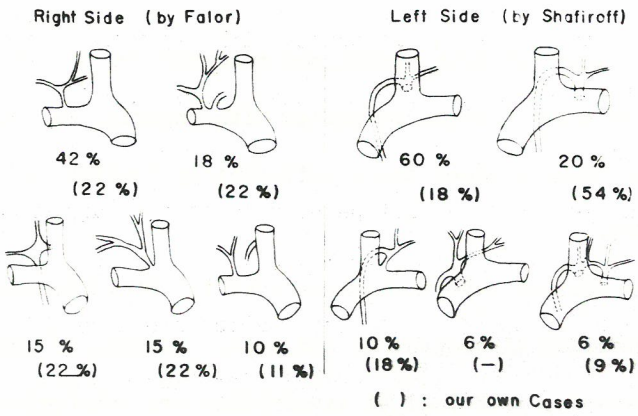

Fig. 2.

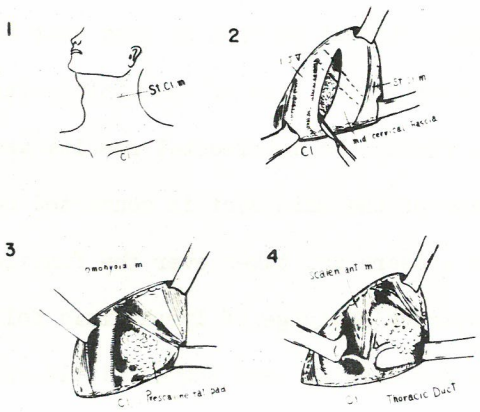

Fig. 3. Exposure of thoracic duct.

appropriate (American made sterilized tube #90 are available (Fig. 7). When the inner surface is coated with heparin, no coagulation of the lymph fluid is seen and a satisfactory function of the tube is maintained.

The cannulation tube must be secured to the surrounding tissue to prevent accidental removal of the tube. Removal of lymph nodes and fat tissue for pathological examination are done prior to the wound closure. In the removal of this fat tissue special care must be taken not to damage phrenic nerve, and suprascaplar artery or transverse colli of this site. The ablation is conducted from the inside towards the outside. Further, it may be added that there is no danger of damaging the carotid sheath, the vagus nerves or the sympathetic chain. It must be kept in mind that twisting or bending of the thoracic duct at the site of cannulation may obstruct the outflow of lymph fluid. No detrimental results are seen even when bilateral ligation of the main duct is conducted because a lymphatico=venous shunt appears and takes over the function. It was also noted that a continous drainage of lymph fluid following thoracic duct cannulation for several days showed little or no awareness on the patients side and no aggravation of the clinical picture.

After completion of the experiment, prior to the removal of the tube, this is clamped and left for 2 days. After waiting for the lymph in the tube to coagulate a simple removal is conducted and a short pressure dressing is made. No complications were seen.

Technique of Thoracic Duct Cannulation

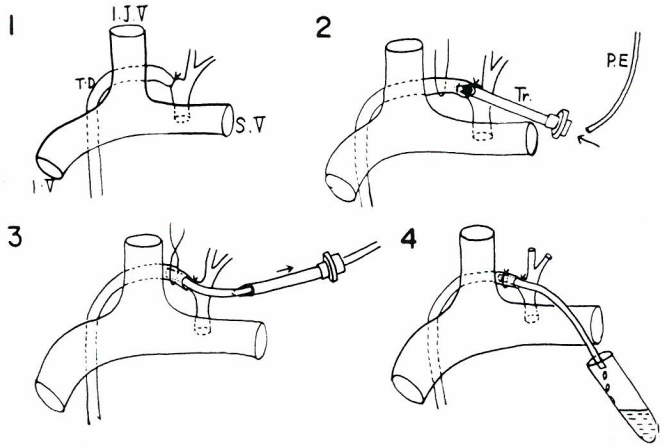

Fig. 4

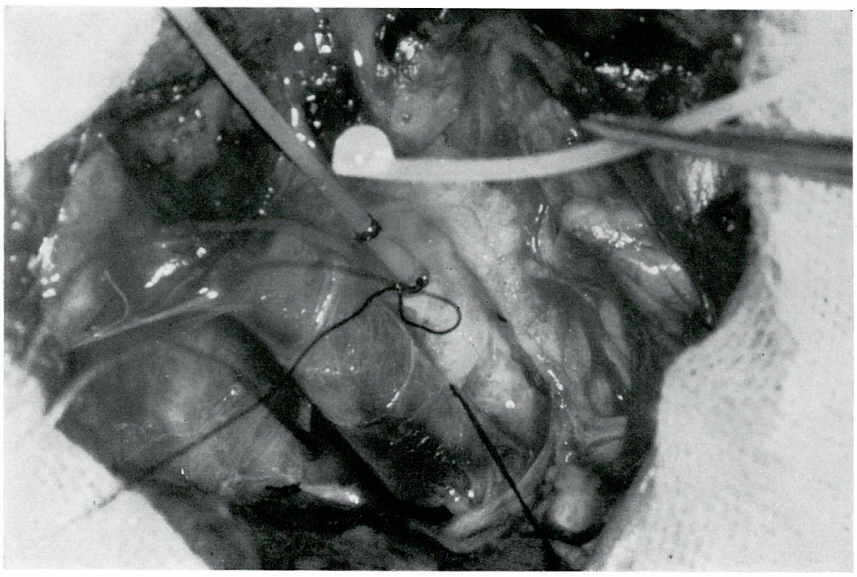

Fig. 5

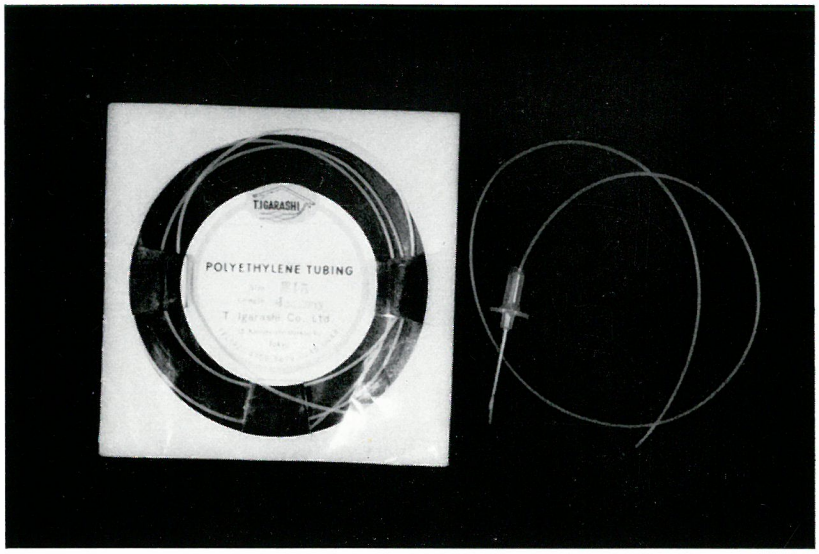
TJGARASHI
POLYETHYLENE TUBING

Fig. 6


STERILE
ANIMAL TESTED
INTRAMEDIC
Polyethylene Tubing
PE-90 S36
I.D. .034" O.D. .050"—36 INCHES
Tubing passes thru 15 gauge needle
20 gauge needle fits into tubing
ELECTRON STERILIZED
IN THE PACKAGE
Sterility not guaranteed if package broken or damaged.
Made in U.S.A.
CLAY-ADAMS, INC.
New York, N. Y.

Fig. 7

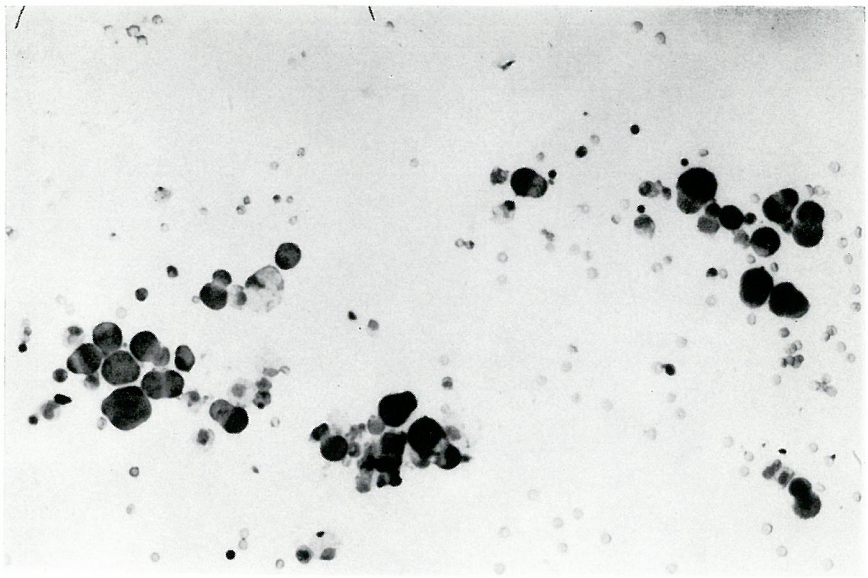

Fig. 8

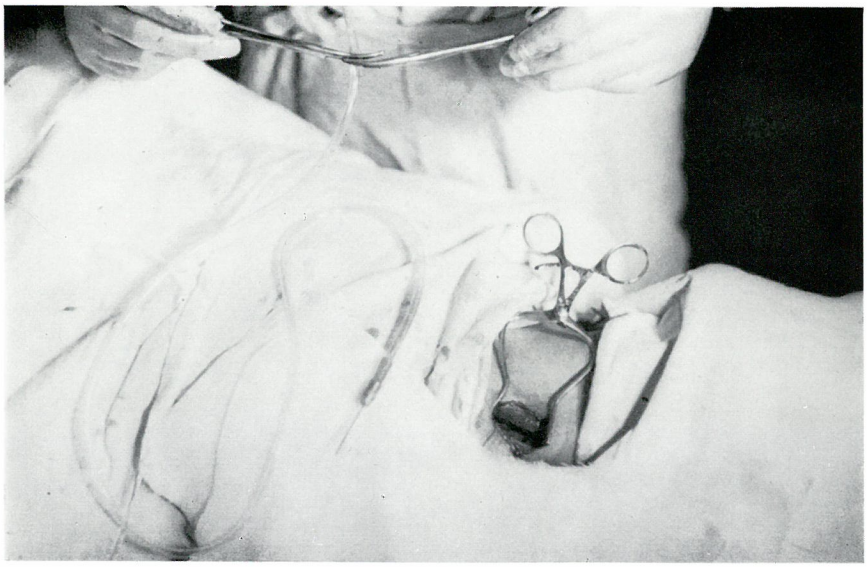

Fig. 9

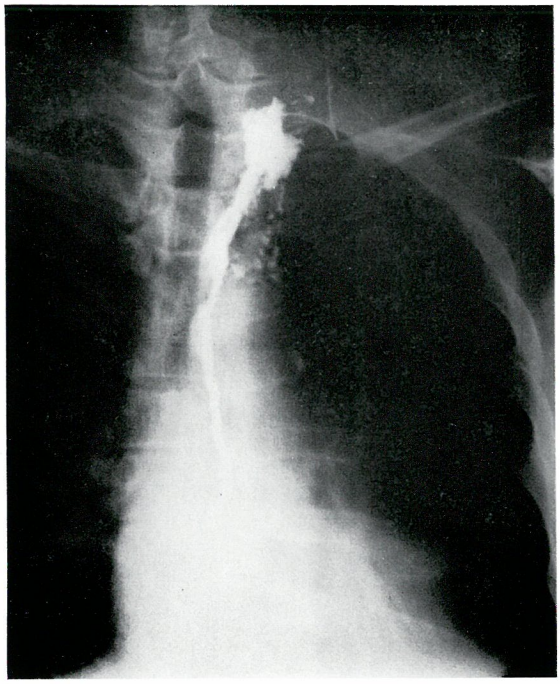

Fig. 10

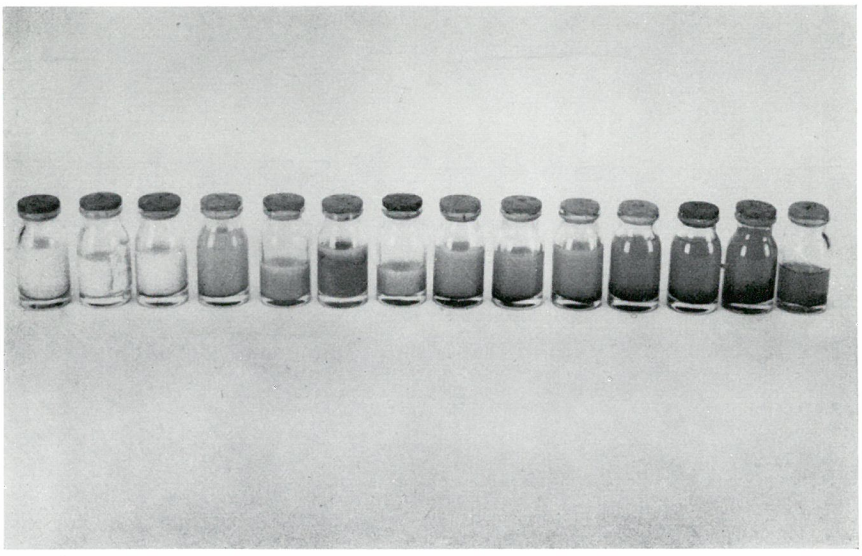

Fig. 11

Complications:

Falor et al. (39), reported the following complications in the presence of thoracic duct cannulation; chyloma, thoracic duct fistula, chylo-thorax, retained polyethylene tube, phrenic nerve paresis, hoarseness etc. However, the authors have not experienced any of the above complications as yet.

Tumor Cell Findings in Thoracic Duct Lymph

In cancer patients, free cancer cells from the cancer tissue appear in the blood stream and at the same time they make their appearance in the lymph flow. To trace the origin of these detached cells in the lymph flow and blood stream and to investigate the course of detachment have a considerable bearing on the diagnosis of the primary cancer and also on the prognosis of the malignancy. Especially in the metastatic course, the detached cancer cells appearing in the blood stream may have originated directly from the cancer tissue itself or may have appeared via the thoracic duct lymph fluid. To determine this, we are conducting investigations using thoracic duct cannulation. In lung cancer operations, some cases show detached cancer cells in the lymph fluid prior to the operation. Thus thoracic duct cannulation may have some bearing on the prevention of control of metastasis coming from operations and may also be utilized in the evaluation of the effectiveness of the operation.

Whereas the possibility that the cancer cell count in the lymph flow may be influenced by operative handling, chemotherapy, radiological therapy has been considered. Watne et al. (41) have reported that in cancer patients subjected to thoracic duct cannulation when given anti=neoplastic agents, show an increase in cancer cell count at 1 hour after which is followed by a drop in the count. In regard to the rate of incidence of cancer cells in the thoracic duct lymph, Young (47) reported 37%, Kausel et al. (49) 30% and Watne et al. (41) 22%. It is considered that the differences may depend on the various stages of the disease. While the rate of incidence in our cases was 33%. It was noted that there was no great difference between the rate of incidence of detached cancer cells in the blood stream. As for the counting of cancer cells, the actual count in lymph fluid was easier than that of the blood stream. The count may be made directly by centrifuge smear methods, but various methods such as removing the blood component and counting the cancer cells have been adopted. We are of the opinion that Foss' method (42) with a 10μ millipole filter, based on the fact that the cancer cells in the blood and lymph form cluster, is superior (Fig. 8).

Retrograde thoracic ductgraphy:

The usefulness of the thoracic duct in surgical treatment was first noted in the treatment of chylothorax (50), (28-30) which led to peripheral lymphangiography and thoracic ductgraphy in thoracotomy. The present authors in an attempt to establish a diagnostic

means for intrathoracic malignancy are investigating the possibilities of retrograde thoracic ductgraphy. The difficulty of thoracic retrograde ductgraphy lies in the presence of valves as in the case of veins. Reports on this are limited. In our clinic a simple infusion apparatus (56) was devised and is in clinical use. As for the contrast media, Ethiodol, lipiodol ultrafluid, or DR 47 (Daiichi Pharmaceutical Corp.) were used. Generally 8 to 10 ml was infused slowly under fluoroscopy over a period of 30 to 45 minutes.

As may be seen in Fig. 10, the retrograde thoracic ductgraphy picture may even suggest mediastinal infiltration caused by malignant tumor because of the obstruction and distortion. However, since this is not the case, this method at present is a mere subsidiary diagnostic means and moreover the contrasting of hilar lymph nodes is difficult. Hence, further work must be done.

Studies on the Composition of Thoracic Duct Lymph

Generally the lymph of the thoracic duct and blood plasma are quite similar in composition except for protein and fat (Table 2). With regard to the protein content of lymph, although it varies under different conditions particulary after meals, the protein concentration in the cervical thoracic duct lymph after receiving the liver lymph flow was 2.5 to 8.0 mg/dl, 0.5 to 0.7 mg/dl in the peripheral lymph and 3.0 to 4.0 mg/dl at the site of cisterna chyli.

Table 2. Composition of Thoracic Duct Lymph

Total Protein	2.5 - 8.0	gm./dl
Albumin	1.2 - 4.5	gm./dl
Globulin	1.0 - 2.8	gm./dl
N.P.N	6.8 - 18.8	mg./dl
Total Cholesterol	115 - 206	mg./dl
Cholesterol Ester	25 - 146	mg./dl
Sugar	103 - 188	mg./dl
Na	112 - 148	mEq/L
K	3.8 - 4.8	"
Ca	4.4 - 5.6	"
Cl	97.2 - 108	"
W.C.C	1000 - 25000	/m³
R.C.C	200 - 8000	/m³

In other words, the protein content of the thoracic duct lymph shows considerably higher values than in the peripheral lymph. When a large volume of lymph fluid is drained over a long period by thoracic duct cannulation, the blood serum protein together with the thoracic duct protein shows low values. Concerning this point Glenn et al. (35) in his experiments reported a complete parallel decrease.

Fat shows the most prominent changes in lymph following meals. Most of the dietary fat consists of triglyceride which are digested in the intestine. Some is absorbed, as is, while the remainder is resynthesized into triglycerides again. After which it becomes a milkish chylo-micro-emulsion and is transfered largely into the lymph duct. Thus, the influence of fat absorption is stronger in

the lymph than in blood. In regard to this an experimental oral administration of fat was made and lymph fluid was led out of the body by thoracic duct cannulation. Even at 5 hours after the ingestion when the blood fat concentration should be at its highest, the volume of fat in the blood showed hardly any difference, whereas the thoracic duct lymph fat concentration showed a 10 to 30 fold increase. Thus, it is apparent that a larger part of the ingested fat is absorbed by the lymph duct. In this case when drainage from the thoracic duct cannulation is discontinued, the fat concentration of the blood plasma shows an increase which seems to indicate the presence of lymphatico-venous communication which commences functioning following the blocking of the thoracic duct. Since orally administered fat commences to increase in the thoracic duct lymph 30 minutes after ingestion, the insertion of the polyethylene tubing is made easy by giving fat rich food 1 to 2 hours prior to the thoracic duct cannulation. The thoracic duct lymph flow varies under the influence of various factors. When the function of the thoracic duct cannulation is sufficient, changes in flow from 10 to 150 ml per one hour or 0.1 to 2.5 ml for 1 minute are seen. Generally, when drainage via thoracic duct cannulation is done for 2 to 6 days an obstruction occurs and the thoracic duct function disappears. Factors influencing the thoracic duct lymph flow, under normal conditions are mainly food especially when water ingestion or fat ingestion increases, the lymph flow increases. In water administration experiments it was shown

that physiological saline solution produced a larger flow than distilled water and it has also been reported that oral administration produces a larger increase in lymph flow than intravenous administration. Likewise in regard to lymph flow changes during operations, it was shown that positive pressure breathing by intubation, postural changes, thoracotomy and vein ligation produced a slight increases in flow. However, with the exception of pressure breathing and pulmonary vein ligation, no remarkable changes were seen in the flow.

Studies on the Lymphatic Drainage in Lungs

In an attempt to follow the mode of drainage of lymph in each lobe, bilateral thoracic duct cannulation was conducted prior to the opening of the chest for lobectomy. Immediately after thoracotomy, Patent Blue V was injected into the parenchyma of the target lobe and the appearance of the dye in the thoracic duct lymph was observed. It was noted that 20 to 30 minutes after infusion the dye made its appearance in the thoracic duct lymph and disappeared at 5 to 6 hours after (Fig. 11). As a result it was revealed that in addition to the corresponding appearance of dye in the thoracic duct on the same side as injected when bilateral infusion was made in the upper lobe, it was noted that the dye infused at the upper right lobe appeared in the left thoracic duct. Similarily, in the bilateral infusion at the lower lobe, in addition to the correspond-

ing appearance of the dye in the thoracic duct on the same side, it was shown that a cross drainage existed to the opposite side which finding seems to differ with that of studies made hitherto. Whether these new findings are due to the specific diffusion of the dye itself or whether a true crossing interchange exists remains unknown.

Conclusion

Owing to the difficulty in operative procedure and other limitations thoracic duct cannulation has not been adopted widely. However, we are of the opinion that thoracic duct cannulation is a highly useful technic for the collection of lymph samples. In addition various clinical applications may be envisioned, and as a diagnostic, therapeutic, and research method it seems that it is a highly useful technic.

Thus in the present paper the clinical significance of thoracic duct cannulation and its operative procedure were introduced together with some findings.

(Received March 15, 1966)

References

1. Fischer, H. W., Lawrence, M. S., & Zimmerman, G. R.: J. A. M. A., 175, 327 (1961).

2. Wallace, S., Jackson, L., Schaffer, B., Gould, J., Greening, R. R. R., Weiss, A., & Kramer, S.: Radiology, 76, 179 (1961).

3. Boyd, A. D. and Altemeier, W. A.: Arch. Surg., 86, 911 (1963).

4. Kinmonth, J. B., Taylor, G. W., & Harper, R. K.: Brit. Med. J., 1, 940 (1955).

5. Kusano, O., Nishishita, M., & Kanasaki, Y.: Nippon Igaku Hoshasen Gakkai Zasshi (Nippon Acta Radiol.), 22, 1353 (1963). (in Japanese)

6. Viamonte, M. Jr., Altman, D., Parks, R., & Blum, E.: Radiology, 80, 903 (1963).

7. Pool, E. H. & Dunlop, G. R.: Am. J. Cancer, 21, 99 (1934).

8. Cole, W. H., Packard, D., & Southwick, H. W.: J. A. M. A., 155, 1549 (1954).

9. Sandberg, A. A., Moore, G. E., & Schubarg, J. B.: Ann. Surg., 146, 580 (1957).

10. Engell, H. C.: Act. Chir. Scand. Suppl., 201, 1 (1955).

11. Fisher, E. R. & Turnbull, R. B.: Surg. Gynec. Obst., 100, 102 (1955).

12. Seal, S. H.: Cancer, 9, 866 (1956).

13. Werner, B.: Act. Chir. Scand. Suppl. 353, (1965).

14. Daniels, A. C.: Dis. Chest, 16, 360 (1949).

15. Shefts, L. M., Terrili, A. A., & Swindell, H.: Am. Rev. Tuberc., 68, 505 (1953).

16. Harken, D. E., Black, H., Clauss, R., & Farrand, R. E.: New Engl. J. Med., 251, 1041 (1954).

17. Connar, R. G.: Surg. Gynec. Obst., 101, 733 (1955).

18. Shields, T. W., Lees, W. M., & Fox, R. T.: Ann. Surg., 148, 184 (1958).

19. Wada, J. & Murai, K.: Shujutsu, 12, 623 (1958). (in Japanese)

20. Lui, A. H. F., Glas, W. W., & Lansing, E. H.: J. Thor. Cardiovasc. Surg., 40, 90 (1960).

21. Christie, S. G. & Stahl, W. M.: Circulation, 30, Suppl., 3, 61 (1964).

22. Rouvière, H.: Ann. Anat. Path. (Paris), 5, 743 (1928).

23. Sabiston, D. C., Archer, G. W., & Blalock, A.: Ann. Surg., 158, 570 (1963).

24. Pressman, J. J. & Simon, M. B.: Surg. Gynec. Obst., 113, 537 (1961).

25. Pomerantz, M., Herdt, J. R. L., Rockoff, S. D., & Ketcham, A. S.: J. Thor. Cardiovasc. Surg., 46, 568 (1963).

26. Moist, A.: Bibliotheca Medica, Anatomie, Heft. 21, Stuttgart, E. Nögele, 1908.

27. Davis, H. K.: Am. J. Anat., 17, 211 (1915).

28. Baldridge, R. R. & Lewis, R. V.: Ann. Surg., 128, 1056 (1948).

29. Hodge, G. B. & Bridges, H.: Surgery, 24, 805 (1948).

30. Meade, R. H., Rapids, G., Head, J. R., & Moen, C. W.: J. Thor. Surg., 19, 709 (1950).

31. Schumacker, H. B. & Moore, T. C.: Surg. Gynec. Obst., 93, 46 (1951).

32. Seaman, J. B.: J. Thor. Surg., 27, 529 (1954).

33. Blalock, A.: Bull. Johnes Hopkins Hosp., 72, 54 (1943).

34. Cain, J. C., Grindlay, J. H., Bollman, J. L., Flock, E. V., & Mann, F. C.: Surg. Gynec. Obst., 85, 559 (1947).

35. Glenn, W. L., Cresson, S. L., Bauer, F. X., Goldstein, F., Hoffman, O., & Healey, J. F.: Surg. Gynec. Obst., 89, 200 (1949).

36. Slaughter, D. P. & Southwick, H. W.: Ann. Surg., 142, 307 (1955).

37. Linder, E. & Blomstrand, R.: Proc. Soc. Expl. Biol. Med., 97, 653 (1958).

38. Schafiroff, B. G. P. & Kau, Q. Y.: Surgery, 45, 814 (1959).

39. Falor, W. H., Meyer, E. G., Bratcher, E., Azarfohimi, A., & Sharp, W. V.: Bull. Akron City Hosp., 4, 1 (1962).

40. Falor, W. H., Bartlett, R. H., Zarafonetis, C. J. D., Dettling, J. J., & LeVernois, E.: Surg. Forum, 14, 242 (1963).

41. Watne, A. L., Hatiboglu, I., & Moore, G. E.: Surg. Forum, 10, 34 (1959).

42. Foss, O. P., Messett, O. T., & Efskind, L.: Surgery, 53, 241 (1963).

43. Flemming, F. & Warnke, H.: Chirurgie, 34, 157 (1963).

44. Landis, E. M.: Am. J. Physiol., 82, 217 (1927).

45. Drinker, C. K.: Lane Medical Lectures. Stanford University, Calif. Stanford University Press (1942).

46. Bieraman, H. R., Byron, R. L., Kelly, K. H., Gilfillan, R. S., White, L. P., Freeman, N. E., & Petrakis, N. L.: J. Clin. Invest., 32, 637 (1953).

47. Young, G. M.: Am. J. Path., 32, 253 (1956).

48. Patterson, R. M., Ballard, C. L., Wasserman, K., & Mayerson, H. S.: Am. J. Physiol., 194, 120 (1958).

49. Kausel, H. W., Reeve, T. S., Stein, A. A., Alley, R. D., & Stranahan, A.: J. Thor. Surg., 34, 631 (1957).

50. Stranahan, A., Alley, R. D., Kausel, H. W., & Reeve, T. S.: J. Thor. Surg., 31, 183 (1956).

51. Correl, N. O. & Langston, H. T.: Surg. Gynec. Obst., 107, 284 (1958).

52. Tunner, W. S., Carbone, P. P., Blaylock, W. K., & Irvin, G. L.: Surg. Gynec. Obst., 121, 334 (1965).

53. Ikeda, K., Kaneko, M., Tsuchida, M., Kitaya, T., & Osawa, T.: Geka, 26, 1307 (1964). (in Japanese)