

8. Hyatt, R. E., G. H. Lawrence and J. R. Smith: Observations on the Origin of Ascites from Experimental Hepatic Congestion. *J. Lab. and Clin. Med.*, **45**:274, 1955.
9. Krogh, A.: *The Anatomy and Physiology of Capillaries*. New Haven, Yale University Press, 1929, p. 307.
10. Prentice, T. C., W. Siri and E. E. Joiner: Quantitative Studies of Ascitic Fluid Circulation with Tritium-labeled Water. *Am. J. Med.*, **13**:668, 1952.
11. Rusznyak, I., M. Foldi and G. Szabo: *Lymphatics and Lymph Circulation*. New York, Pergamon Press, Ltd., 1960.
12. Taylor, F. W.: Experimental Portal Hypertension. *Ann. Surg.*, **146**:683, 1957.
13. Starling, E. H.: The Influence of Mechanical Factors on Lymph Production. *J. Physiol.*, **16**:224, 1894.
14. Starling, E. H.: *The Fluids of the Body*. Chicago, W. T. Keener, 1909.

#### DISCUSSION

DR. JAMES D. HARDY (Jackson, Miss.): I did not have an opportunity to see the manuscripts ahead of time, but I believe we have evidence which will reinforce some of the important information which has been described to you.

Dr. Fikri Alican and I have studied various aspects of the thoracic duct, intestinal, and hepatic lymph flow, in some respects paralleling the work of Drs. Dumont and Mulholland.

(slide) May I say, Dr. Litwin and Dr. Cope, that this graph presents data which provide additional evidence that thoracic duct lymph flow does, in fact, increase in hemorrhagic shock. Each one of these cross bars represents a drop of thoracic duct lymph falling into a carefully constructed measuring device, and it may be seen that as the blood pressure of the dog declined following bleeding, there was an increasingly rapid rate of lymph flow.

(slide) This diagram presents endotoxin shock to be compared with the hemorrhagic shock which was previously mentioned. Note that when endotoxin was injected intravenously, there was an initial rise and then a more delayed or secondary rise in the rate of thoracic duct lymph flow. When the portal vein pressure increased, the thoracic lymph flow increased, even though the systemic arterial pressure had usually declined. This initial increase in portal vein pressure and thoracic duct lymph flow following the injection of endotoxin was abolished by portacaval shunt. The more delayed or secondary rise in thoracic duct lymph flow, which usually followed the injection of endotoxin, was not abolished by portacaval shunt and was considered to be due to capillary damage in the splanchnic bed.

(slide) The next slide presents clinical findings in a spectacular case. Operated upon for portal hypertension with esophageal hemorrhage and ascites, this man had an enormous number of lymphatic channels emerging from the hilum of the liver. One of these channels, almost 1.0 cm.

in diameter, was ligated and divided to gain access to the vena cava and the portal vein. Some minutes after it had been ligated, it ruptured spontaneously on the pancreatic side, and lymph spurting several centimeters vertically was easily collected in a specimen cup. This spontaneous rupture due to a build-up in pressure suggested that a similar mechanism may be invoked to explain spontaneous chylothorax which develops in association with malignant tumors. This patient lost from 1.0 to 2.0 liters of lymph into the abdomen during the course of the shunt operation, largely from unnumberable lymphatic vessels of various sizes, with relatively little venous oozing.

(slide) Lastly, the management of a clinical problem will be mentioned. This slide illustrates the procedure used in the operative closure of a thoracic duct fistula which developed in an infant following division of a patent ductus. Using the technic described by Drs. Cohn and Strug, it was the soul of simplicity to inject the Sky Blue dye (Wyeth) into the wall of the esophagus, massage the epigastrium and have the defect in the thoracic duct beautifully delineated. The duct was ligated on both side of the perforation, the lung was decorticated, and the infant went home in a week. It is recommended that postoperative thoracic duct fistulas be closed by early re-operation, if the chylothorax does not recede within a few days.

DR. HOWARD A. FRANK (Boston): Dr. Litwin and Dr. Cope were kind enough to show me their plans for these experiments and I wish to express admiration both for the skill in which they were carried out and for the important data they have furnished. The contribution of lymph circulation to the restoration of plasma volume after hemorrhage has received little attention. Dr. Litwin's nicely delivered paper shows us that this neglected mechanism, by restoring plasma protein to circulation, may well be more important than the reabsorption of fluid through the capillary membrane.

DR. JOHN H. MULHOLLAND (New York): It is apparent from these reports by Drs. Litwin and Dumont that more consideration must be paid in hemodynamic studies to the lymphatic system for collection of fluid and large molecules. Both speakers extended observations made by Starling many years ago.

Dr. Dumont showed that the relationship between intravascular flow and pressures in hepatic vascular circulation and in hepatic lymph pressures are strikingly synchronous with changes in intravascular pressures. Dr. Litwin very lucidly described the role of lymphatics in restoring large molecules which have escaped from capillaries back into the blood. In hepatic cirrhosis it appears that the escaping particles can be as large as a red cell since hepatic lymph in patients with cirrhosis, as Dr. Dumont told us, always contains intact red cells.

Without direct relevance to the subject of the papers I would like to relate an experiment which Dr. Dumont performed in connection with these studies. On the basis of his idea that the antigens produced by a homograft would be large molecules transported in lymph he homografted skin under the capsule of the kidney in dogs and drained the lymph off through a cannula in the thoracic duct. The skin homotransplants survived intact throughout the period of drainage, in some animals now persisting for more than five weeks.

The lymphatic system has long been disregarded as an important feature of homeostasis, of circulatory dynamics and, as has been shown here today, as a background for the mysterious hemodynamic changes which are a prominent feature of hepatic cirrhosis.

DR. OLIVER COPE (Boston): The neurosurgeons stole the show from the lymphatic system by terming the spinal fluid the third circulation. I do not mean to minimize the importance of the spinal fluid—I believe it important—but in terms of the function of most organs, lymph is by all odds the largest third circulation. These two papers develop the aspects of why lymph is important.

Cecil Drinker pointed out the importance of the lymphatic circulation in his monumental work, and we surgeons have been slow in visualizing it. A certain amount of albumin and other protein is constantly leaking out of the capillaries. This leakage is inevitable since capillaries cannot be absolutely semipermeable—there is not any other way. Vascular protein is thus puddled in the interstitial space. From there it is very slowly recaptured and returned to the vascular tree where it again forms the colloid needed for the maintenance of blood volume and blood pressure.

It was this circulation of protein and fluid that Drinker stressed as an essential part of the fluid equilibrium of the body. In this morning's paper, Dr. Zimmerman in discussing the paper on hem-

orrhage pointed out, very correctly, exactly what Bert Litwin has shown on his slide—that there is within five minutes a slight dilution of both hematocrit and plasma protein. This dilution is the Starling effect. That is all the Starling effect can do, because as soon as the plasma volume is slightly increased, then the blood pressure rises and filtration begins again. The two cancel each other out.

The only way that one can bring out a sizable replenishment of the blood volume is by adding protein and the reservoir for that protein is the 50 per cent puddled outside the vascular tree. This large exchange of protein is why the lymphatic system ought to be called the third circulation.

Dr. Litwin's observations also explain Dr. Fine's discussion this morning, to go back to the paper on hemorrhage. Dr. Fine was right in saying that the patient he saw in London needed plasma—but his reason was wrong. He assumed that there must be continuing plasma leakage out into the wound area. Well, there may have been a certain amount leaking out but it was not as much, probably, as that patient needed. And why?

When a patient has a hemorrhage and needs plasma protein to rebuild the plasma volume, this protein is taken out of the reservoir in the interstitial space; but the patient now has a deficit in the interstitial space. Every gram of protein that is returned to rebuild a plasma volume depletes the interstitial space by just one gram. If the patient who has a hemorrhage does not have prompt therapy, including plasma protein as well as red cells, his reservoir and his normal equilibrium of plasma protein, the fountain that is going out and then coming back into circulation, becomes depleted and this is what upsets the water and electrolyte dynamics. This is exactly what we wanted to stress, so I thank Dr. Fine, also.

Dr. Dumont's observations were just marvelous because, again, he showed how essential a part of the circulation the lymphatics are. Look at what he demonstrated for us! It is also good news that Dr. Hardy and his colleagues have begun investigating the lymphatics, joining Dr. Mulholland and Dr. Dumont and the New York University group.

DR. J. ENGLEBERT DUNPHY (Portland, Oreg.): I wonder how much the liver contributes. The liver must be making protein all the time. Perhaps Dr. Litwin will answer that.

DR. R. KENNEDY GILCHRIST (Chicago): I want to ask two questions of the essayists. 1) What effect does the intravenous or subcutaneous injection of so-called physiologic salt solution have on the amount and the character of the lymph flow from this duct, both the rapid and slow injection? and 2) What effect does intragastric or intrasmall bowel suction have on this flow?

DR. S. BERT LITWIN (closing): In reference to your question, Dr. Dunphy, I suspect that probably the liver does add something. It is an unsettled question as to whether all of the protein is preformed or new. I think probably it is a combination of both.

Dr. Gilchrist brought up a nice point. In some of the dogs we have observed, if rapid infusion of intravenous saline is given there is an immediate increase in thoracic duct lymph flow. I suspect that the subcutaneous injection of saline might do the same, and have wondered whether this might help to flush out the interstitial space protein that is there at the time of hemorrhage. I think this is a very good point and is something in which we are interested.

I cannot answer the question concerning the small bowel content.

DR. ALLAN S. DUMONT (closing): We have followed Dr. Cope's lymph studies with great interest for a long time, especially his work on lymph

flow in burns. Dr. Blalock's studies of the effect of constrictive pericarditis on lymph pressure and lymph flow, carried out almost 30 years ago, seem especially significant today.

We were very interested in Dr. Hardy's chance observation that troublesome bleeding during a portacaval shunt seemed to be modified by drainage of excess lymph from a spontaneous lymph fistula. This would fit in with our present notions about some interrelationships between pressure in the portal system and adequacy of lymph flow.

So far as Dr. Gilchrist's question is concerned, we think that it has been shown quite adequately that saline infusions, glucose and water, and certain other materials, all have an almost immediate and direct influence on rate of flow from a cannulated thoracic duct; they increase it.

We do not know what the effect of small bowel suction is on lymph flow. There is some evidence that hyperperistalsis, on the other hand, significantly increases flow through the thoracic duct.

---

## Erratum

In the paper by Dr. E. Converse Peirce, II, published in *Annals of Surgery*, July 1962, pp. 138-146, three illustrations inadvertently were transposed. Readers should be informed that Figure 2 should have been identified as Figure 3; Figure 3 should have been Figure 4; and Figure 4 should have been Figure 2.