EDITORIAL

Influence of Mechanical Factors on Ascites Formation in Hepatic Cirrhosis

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In 1896, Starling first proposed that transcapillary fluid exchange and lymph formation are governed primarily by a balance of mechanical forces. Whereas capillary hydrostatic and tissue colloid osmotic pressure tend to shift fluid into tissues, plasma colloid osmotic and tissue hydrostatic pressure tend to maintain fluid within the vascular compartment. Furthermore, Starling recognized that when circumstances favor increased capillary transudation, edema is not inevitable because of a compensatory increase in lymphatic flow. "Dropsy", he stressed, ultimately depends on an excess of lymph production over lymph absorption (1).

In hepatic cirrhosis, lack of good correlation between the presence of ascites and the level of portal venous hydrostatic pressure and plasma colloid osmotic pressure has led to the view that factors other than those considered by Starling are of paramount importance in the formation of ascites. However, as knowledge has not been available until recently concerning the forces on the other side of the capillary membrane and the magnitude of lymphatic drainage in the liver and extrahepatic portal bed, the validity of Starling's concept in the genesis of ascites could not be fully examined.

Thoracic duct lymph, a fluid derived almost entirely from the liver and extrahepatic portal bed, is formed in great excess in patients with cirrhosis whether or not ascites is present (2, 3). When resistance to venous outflow from the liver (postsinusoidal block) predominates, capillary hydrostatic pressure in the liver rises. As hepatic sinusoids are highly permeable to plasma protein, despite collagenous thickening of the sinusoidal endothelium in some cirrhotic livers, the colloid osmotic pressure gradient (effective plasma colloid osmotic pressure) across the hepatic sinusoid is minimal. Capillary filtration is favored and increased formation of hepatic and thoracic duct lymph, *high in protein* follows (3). On the other hand, when resistance to portal venous flow into the liver develops (presinusoidal block), hydrostatic pressure in less permeable extrahepatic portal capillaries increases filtration of water and solute disproportionately compared with protein. Splanchnic tissue protein concentration falls precipitously (3) and the absorbing property of plasma protein is enhanced, limiting further capillary filtration from rising portal venous pressure. Thus, despite a reduction in the *absolute* level of plasma colloid osmotic pressure in many cirrhotics, *effective* plasma colloid

osmotic pressure across the extrahepatic portal bed is considerably higher than normal (4). The observation that thoracic duct lymph flow is elevated in all stages of cirrhosis indicates that the driving force of portal hypertension outweighs the compensatory rise in effective plasma colloid osmotic pressure in the liver and extrahepatic portal bed.

The appearance of ascites, on the other hand, means that increased lymph flow has not kept pace with increased production of lymph and that some of the excess has spilled into the peritoneal cavity. Moreover, the protein content of ascitic fluid and/or thoracic duct lymph depends upon the major source of excess lymph (high protein content from the liver or low protein content from the extrahepatic portal bed) and, therefore, upon the predominant derangement in portal circulatory dynamics (post or presinusoidal block) (3, 5). The discrepancy between the amount of lymph formed and the amount of lymph returned to the blood stream, represented in part by the pool of ascitic fluid, reduces the "effective arterial volume" and sets into motion a series of homeostatic adjustments resulting in salt and water retention (6). Plasma volume is temporarily restored, capillary hydrostatic pressure rises, and more fluid is forced out of the vascular space. The lymphatic circulation is further overloaded and ascites increases. In contrast, diuretic therapy or dietary salt and water restriction contract intravascular volume and probably reduce lymph formation: ascites decreases or disappears. A portacaval shunt drastically lowers hydrostatic pressure in the extrahepatic portal bed and to a variable extent in the liver (3). Reduction of the major driving force promoting increased transudation in these beds decreases lymph formation and relieves salt and water retention: ascites usually disappears. The fact that ascites may persist or reappear after this operation does not mitigate against Starling's theory. Rather it implies that intrahepatic portal hypertension has not been completely relieved (postsinusoidal block persists), that numerous large transected periportal hepatic lymphatics are leaking, or that the shunt is occluded or hemodynamically ineffective (7). Although measures for alleviating ascites are ordinarily directed at reducing lymph *production*, acceleration of lymph *absorption* should also relieve ascites. That this is indeed the case is supported by maneuvers to potentiate lymph flow by internal or external diversion of the thoracic duct (2, 8).

At the turn of the century, a number of observations about lymph formation seemed inexplicable in terms of known mechanical forces, and for this reason, "metabolic derangements" and "secretagogues" were invoked to resolve the discrepancy. The work of Starling, and later *Landis* and *Pappenheimer*, demonstrated that what appeared paradoxical or inconsistent was actually quite comprehensible in terms of the net balance between capillary and tissue hydrostatic and colloid osmotic pressures on the one hand and lymph absorption on the other. More recently, in an effort to explain a number of perplexing observations concerning cirrhotic ascites, it is fashionable to refer to metabolic derangements ("liver decompensation" and "failure") or secretagogues "circulating humoral factors"). However, information that is now available in patients with hepatic cirrhosis on the magnitude of the mechanical forces operating on both sides of the capillary membrane and the capacity of lymphatic drainage suggests that the pathogenesis of ascites in this disorder is in keeping with Starling's original concepts.

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X-Ray Opacification of Hepatic Lymph Nodes Following Intravenous Injection of Tantalum Dust*

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Available methods for x-ray opacification of lymph nodes rely upon either an intraperitoneal or an intralymphatic injection of contrast material. Intraperitoneal injection leads to opacification of intrathoracic, internal mammary nodes while injection into a peripheral lymphatic results in opacification of regional nodes. A successful attempt to obtain x-ray visualization of hepatic lymph nodes following intravenous administration of contrast material forms the basis for this preliminary report. The method depends upon the uptake of radiopaque powdered tantalum by the liver and subsequent transport of tantalum in hepatic lymph.

Method

Fresh suspensions of tantalum powder* (particle size averaging 2.5 microns) were prepared as follows: 200cc of 10% sorbitol were added to 50 grams of tantalum powder, stirred for 1 hour in a Vertis homogenizer and immediately injected intravenously in

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* The tantalum used in this study was obtained from the Fansteel 1 Tantalum Place, Chicago, Illinois.