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EDITORIAL REVIEW

Role of peritoneal cavity lymphatic absorption in peritoneal dialysis

The number of patients with end–stage renal disease on peritoneal dialysis therapy continues to increase [1]. Although transcapillary peritoneal transport of water and solutes in CAPD has been widely studied since its inception in 1976 [2, 3], the role of lymphatic absorption from the peritoneal cavity in peritoneal dialysis has been neglected. Calculations of mass transfer of solutes are based on the observed drainage volume and dialysate solute concentration. Removal of water and sodium in peritoneal dialysis is dependent on the net ultrafiltration volume at the end of the exchange. Assuming residual volume remains constant, the drain volume after a peritoneal dialysis exchange is equal to the infused dialysate volume plus net transcapillary peritoneal transport of water and solute, minus cumulative lymphatic absorption during the dwell time (Fig. 1); the ultrafiltration volume is equal to net transcapillary ultrafiltration minus lymphatic drainage during the dwell time. Consequently, disregarding the reduction in drain volume due to lymphatic drainage can cause considerable errors in calculating actual peritoneal transport in physiological experiments and, more important clinically, excessive lymphatic absorption may be a significant factor in the loss of ultrafiltration observed in some CAPD patients. This review aims to summarize current knowledge of the anatomy and physiology of the peritoneal cavity lymphatics and to provide evidence which supports the concept that cumulative lymphatic absorption during long–dwell, peritoneal dialysis exchanges reduces net ultrafiltration volumes and solute clearances.

Anatomy

Lymphatic drainage of particles, red blood cells and labelled plasma protein from the peritoneal cavity occurs mainly from end lymphatics (stomata) located in the diaphragm, especially in the right half around the liver [4–6]. Absorption through the rest of the parietal peritoneum, mesenteric, and omental lymphatics contributes a small proportion of total peritoneal lymphatic drainage [6–8]. Stomata on the peritoneal surface of the diaphragm were first observed over a century ago by von Recklinghausen [9] and the presence of these specialized end lymphatic openings has since been confirmed by scanning and transmission electron microscopy [10–12]. The lymphatic stomata are triple–layer composite structures consisting of mesothelium, a loose network of connective tissue, and endothelium through which particles and colloids pass to the lacunae of lymphatic capillaries [10, 12]. The intercellular gaps that develop between the mesothelial and endothelial cells adjacent to stomata [10, 12] and the fenestrations in the submesothelial connective tissue and basement membrane [13] permit absorption via an extracellular pathway, although vesicular transport may also occur [12]. The lymphatic capillaries coalesce to form collecting lymphatics and prenodal lymphatic trunks. Most of the lymphatic trunks from the diaphragm travel retrosternally along with the internal mammary arteries to the anterior mediastinal lymph nodes and return 80% of the peritoneal lymphatic drainage to the venous circulation via the right lymph duct [7, 14]. The lymphatic drainage from the remainder of the peritoneum, including part of the diaphragm, is returned to the bloodstream via the thoracic duct [7]. Cannulation of the thoracic duct during peritoneal dialysis in animals collected less than 30% of total peritoneal lymphatic drainage [15, 16]. Obstruction of both the right lymph duct and thoracic duct does not prevent all intraperitoneal labelled protein from returning to the blood [7], and suggests that other small lymphatico-venous communications remain intact. These lymphatic pathways of absorption of intraperitoneal fluid are summarized in Figure 2.

Function

The lymphatics act as a one–way system which returns excess interstitial and serous fluid to the blood vascular system. Water may transfer across the peritoneal capillaries in either direction, depending on the hydrostatic and oncotic (colloid osmotic) pressure gradients between the blood and interstitium. Net transcapillary pressure (ΔP) may be written:

$$\Delta P = (P_c - P_p) - (\pi_c - \pi_p);$$

where P_c = capillary hydrostatic pressure, P_p = hydrostatic pressure in the peritoneal interstitium, π_c = oncotic pressure in the capillaries and π_p = oncotic pressure in the peritoneal interstitium. Movement of water from interstitium to the peritoneal cavity will depend on the same pressure forces across the mesothelium separating the fluid in the peritoneal cavity from the interstitium. Bidirectional transfer of small solutes occurs by diffusion along the concentration gradient and by solvent drag.

Large colloid molecules of molecular weight greater than 20,000 exhibit transperitoneal transport asymmetry [17] and thus minimal direct absorption into the capillaries. After unidirectional transport from capillaries by filtration through large pores and/or pinocytosis [17, 18] macromolecules such as albumin are transported back from the peritoneal interstitium and cavity to the venous circulation by the lymphatics [19, 20]. Such is the importance of lymphatic absorption of interstitial protein that it has been estimated that 50% of the total blood protein is returned from the tissue spaces by the lymphatic system each day [21], and in hepatic cirrhotics with ascites,

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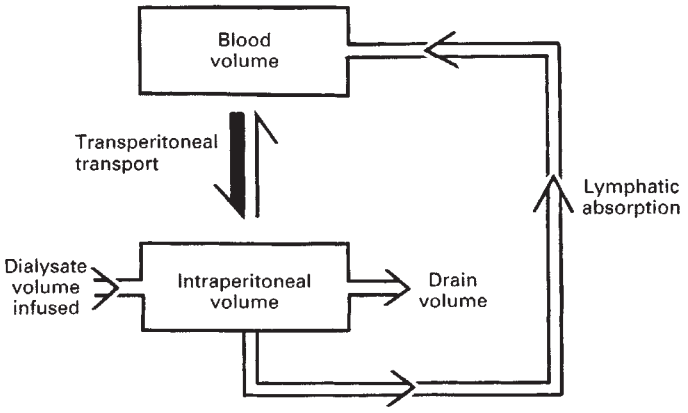

Fig. 1. *Solute and water transport in peritoneal dialysis.* Solute mass transfer for solutes not initially present in the dialysis solution equals drained dialysate solute concentration × drain volume (drain volume = dialysate infusion volume + net transcapillary transport − lymphatic absorption during dwell time). Ultrafiltration volume equals net transcapillary transport − lymphatic absorption during dwell time.

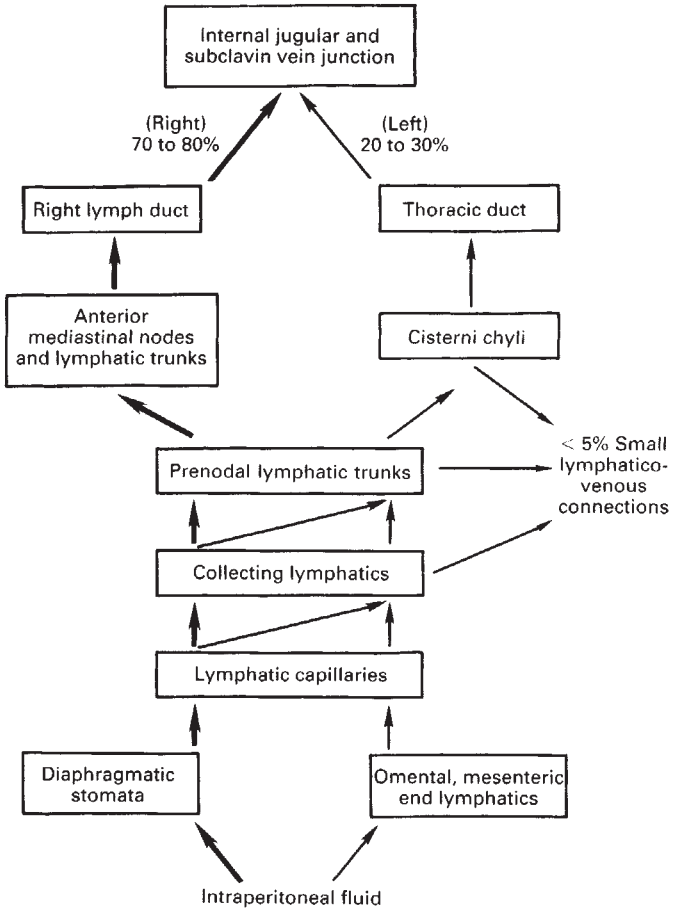

Fig. 2. *Anatomical pathways of lymphatic absorption of intraperitoneal fluid.* Lymph returns to venous circulation via (R) lymph duct (70 to 80%), thoracic duct (20 to 30%) and small lymphatico-venous junctions (< 5%).

9 · 6% of the intravascular protein mass is returned to the bloodstream from the peritoneal cavity each day [22]. Since lymphatic drainage of tissue or serous fluid normally equals its rate of formation, interstitial edema or serous effusions do not develop and only a small volume of isosmotic fluid is normally maintained in the peritoneal cavity.

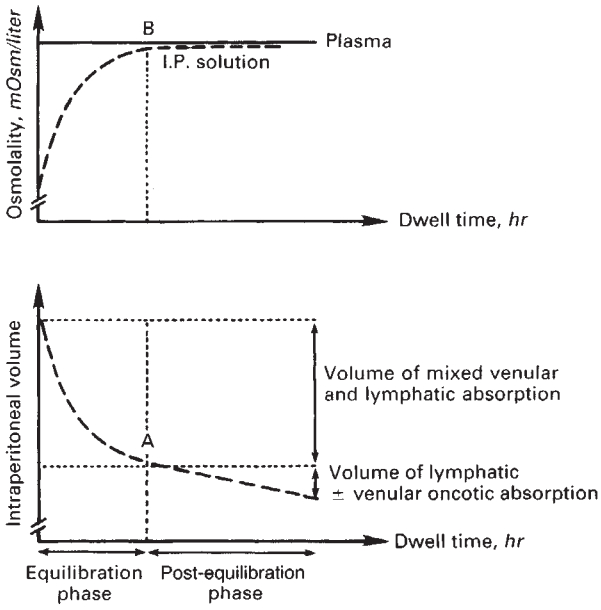

Fig. 3. *Changes in osmolality and intraperitoneal fluid volume after infusion of 0·9% NaCl.* Equilibration volume (point A) coincides with crystalloid osmotic equilibrium (point B). Mixed venular absorption refers to fluid absorption due to both crystalloid and colloid osmotic pressure.

Intraperitoneal fluid kinetics

Solute and water kinetics have been studied when isotonic and hypertonic solutions are instilled in the peritoneal cavity. When isotonic saline solution was infused intraperitoneally in three uremic subjects [23] and in 11 dehydrated dogs [24], the initial rapid, transcapillary fluid absorption gradually decreased until transperitoneal osmotic equilibrium was reached (Fig. 3). Thereafter the isosmotic fluid was absorbed at a constant rate of 33 ml/h in man [23] and 16 · 8 ml/h in the dog [24]. This absorption phase is thought to be mainly due to peritoneal lymphatic drainage.

In contrast, hypertonic dextrose solutions are routinely used in peritoneal dialysis, and the crystalloid osmotic pressure-gradient predominates and alters transcapillary pressure to induce ultrafiltration. That is:

$$\Delta P = (P_c - P_p) - (\pi_c - \pi_p) - (O_c - O_p)$$

where O_c = crystalloid osmotic pressure in capillaries and O_p = crystalloid osmotic pressure in the peritoneal interstitium. Movement of ultrafiltrate into the peritoneal cavity would depend on similar relationships of interstitial to peritoneal cavity pressure-gradients. The peritoneal membrane is not equally permeable to all solutes in dialysis fluid and thus the osmotic pressure gradient is the sum of the products of the reflection coefficient and concentration gradient for each solute. Since ultrafiltration occurs, water and solute movement from peritoneal capillaries into the peritoneal cavity by way of pathways through the interstitium must bypass absorption by the interstitial lymphatics. In fact, some ultrafiltrate might come

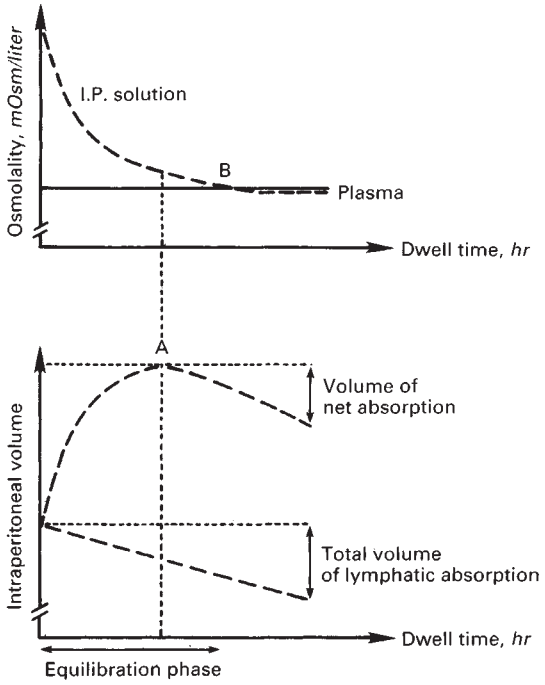

Fig. 4. *Changes in osmolality and intraperitoneal fluid volume after infusion of 2·5% dextrose dialysis solution.* Peak intraperitoneal volume (ultrafiltration) represented by point A precedes crystalloid osmotic equilibrium (point B). At peak ultrafiltration, lymphatic absorption rate equals transcapillary ultrafiltration rate.

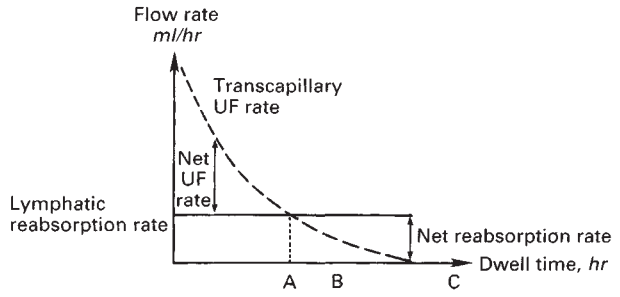

Fig. 5. *Net ultrafiltration (UF) and lymphatic reabsorption rates during 2·5% dextrose dialysate dwell.* Lymphatic reabsorption is assumed to be constant. Point A represents maximum intraperitoneal volume when the net ultrafiltration (UF) rate is zero. Point B indicates time when dialysate/plasma osmolality ratio is 1, and point C represents time when dialysate/plasma glucose is 1.

from interstitial lymphatics subsequent to the osmotic effects of interstitial glucose.

In peritoneal dialysis the net transcapillary ultrafiltration rate is maximum at the onset of the exchange and decreases exponentially as the crystalloid osmotic pressure–gradient dissipates. The intraperitoneal volume increases until it reaches a maximum when the rate of transcapillary transport equals the rate of peritoneal lymphatic absorption (Fig. 4). After peak ultrafiltration, transcapillary efflux continues at a slow rate until crystalloid osmotic equilibrium is approached later in the dialysate dwell time. Net reabsorption begins when the lymphatic absorption rate exceeds the transcapillary ultrafiltration rate and continues after crystalloid osmotic equilibrium. Under both of the above conditions fluid flux during the equilibration phase is primarily dependent on the crystalloid osmotic pressure gradient since intravascular hydrostatic pressure, capillary oncotic pressure and peritoneal permeability/area remained relatively constant. For any given patient on peritoneal dialysis, increases in osmolality of the dialysate result in prolongation of the time until crystalloid osmotic equilibrium is achieved, increase in peak ultrafiltration volume, and delay until net intraperitoneal fluid reabsorption begins [25, 26], even though the lymphatic absorption rate is unlikely to have decreased.

Osmotic equilibrium is first reached in peritoneal dialysis before glucose equilibrium since there is sieving of small solutes with ultrafiltration [2]. Further net transcapillary absorption of dextrose occurs because of the glucose concentration gradient. Simultaneously there is transcapillary net efflux of small solutes (sodium, potassium, urea, phosphate) because of concentration gradients subsequent to sieving. After crystalloid osmotic equilibrium, there may be a transient phase where dialysate is low in electrolytes due to mixing with low electrolyte ultrafiltrate and dialysate is hypoosmolar to serum. In this same phase, dialysate glucose may still exceed serum glucose, and because of the higher reflection coefficient for glucose compared to other smaller solutes [27], some net transcapillary ultrafiltration continues. Hence intraperitoneal net fluid reabsorption near osmotic equilibrium initially represents lymphatic absorption in excess of transcapillary ultrafiltration (Fig. 5). Later, Gibbs–Donnan equilibrium is approached, net transcapillary ultrafiltration falls to zero and venular reabsorption begins due to serum oncotic pressure. Late phase reabsorption has been reported to average 37 ml/hr (range 8 · 3 to 89 · 2 ml/hr) [26]. Although transcapillary (venular) fluid absorption due to transmembrane oncotic pressure near crystalloid equilibration is likely to be minor, lymphatic absorption in peritoneal dialysis, unlike the above studies with isotonic solutions [23, 24], cannot be assumed to equal the rate of decrease of intraperitoneal volume after maximum ultrafiltration since this rate represents lymphatic flow minus net transcapillary ultrafiltration. Thus the lymphatic absorption rate in peritoneal dialysis should be calculated directly.

Calculation of lymphatic absorption

The measurement of the peritoneal lymphatic flow rate is dependent on certain assumptions:

1. Isosmotic intraperitoneal fluid is drained by the peritoneal lymphatics without increase or decrease in protein content [16, 22, 28–30].
2. Intraperitoneal red cells [14, 16] and macromolecules of molecular weight greater than 20,000 [16, 17], such as albumin [7, 31, 32], are returned to the venous circulation exclusively by the peritoneal lymphatics.

Hence the peritoneal lymphatic absorption rate can be calculated from either the rate of mass transfer of labelled colloids and red cells from the peritoneal cavity to the blood or from their rate of disappearance from the peritoneal cavity. Peritoneal to plasma clearance of tracer may be written:

$$F_L = \frac{V_D \times \Delta C_D}{C_P}$$

where F_L = total peritoneal lymphatic flow during time of study;
V_D = volume of distribution (blood volume);
ΔC_D = rise in tracer concentration in blood volume;
C_P = average intraperitoneal tracer concentration.

By this method, intraperitoneal radio-iodinated serum albumin (RISA) [22, 33, 34] and radio-colloid [34–36] have been used to measure lymphatic flow rates in hepatic [22, 34], malignant [34–36] and nephrogenic ascites [33]. Adequate intraperitoneal mixing [33] of the tracer and intra-individual reproducibility [34] of these methods have been shown. After an initial lag phase radiolabelled protein concentrations in the blood increase linearly with time [22, 33, 34] as predicted. However, all of the absorbed tracer cannot be recovered from the blood [16]. Radiolabelled proteins, but not red cells, are redistributed out of the blood volume [16] and so their elimination rate (K_{ELIM}) from the blood compartment after intravenous administration should be included in order to calculate the lymphatic absorption rate more accurately [16, 17]. Intact human red-blood cells ($7 \cdot 2\ \mu$ diameter) are readily absorbed by the peritoneal lymphatics [14], and K_{ELIM} = zero [16]. However red cells (and particles) may be fixed by omental macrophages and lymph nodes [37] and are absorbed at a slower rate than plasma when compared in the rat [16]. Since lymphatic penetrability is less in man [38] than in the rat (lymphatic uptake of plastic spheres up to 24 μ diameter [13]), the rate of peritoneal lymphatic absorption is even more likely to be underestimated in man when measured using labelled red cells. Estimates of peritoneal lymphatic flow rate by this method [16], are consistently lower than direct observation of absorption of intraperitoneal plasma or blood [4].

Alternatively the peritoneal lymphatic absorption rate may be calculated from the rate of loss of tracer colloid from the peritoneal cavity [16]. That is:

$$F_L = \frac{(IPV_0 \times C_0) - (IPV_t \times C_t)}{C_p}$$

where F_L = total peritoneal lymph flow during time t;
IPV_o & IPV_t = intraperitoneal fluid volumes at times 0 and t;
C_o & C_t = intraperitoneal tracer concentrations at times 0 and t;
C_p = geometric mean intraperitoneal tracer concentation.

This method avoids errors in calculating lymph flow due to delayed transfer of tracer from the submesothelial interstitial lymphatics and diaphragm to the blood (16). The disadvantages of this method are errors in estimating intraperitoneal volumes and the need for serial samples of intraperitoneal fluid. The latter is easily achieved in peritoneal dialysis since the patients have peritoneal catheters in situ, and we are currently applying this method in our institution.

Despite ligature of both the right lymph and thoracic ducts, a small amount of intraperitoneal dye–protein enters the blood [39], suggesting either direct absorption of the dissociated label [39], the presence of unobstructed small, accessory lymphatico–venous connections [7], or a small exchange of protein directly from tissue fluids into the blood capillaries [40]. This may equally apply to tracers used in both of the above methods of calculating lymphatic absorption. Hence neither labelled red cells nor proteins fulfill all of the criteria listed in Table 1 for an ideal indicator of the rate of mass lymphatic transfer from the peritoneal cavity. In general lymphatic flow rates measured by the appearance of an indicator in the blood tend to be underestimated whereas the disappearance rate of an indicator from the peritoneal cavity tends to overestimate lymphatic absorption. Despite these limitations, a number of variables have been shown to influence the lymphatic flow rate, determined by the above methods, and these factors have important implications for the mechanism of peritoneal lymph formation.

Table 1. Criteria for an ideal indicator–dilution method of calculating peritoneal lymphatic flow rate

1. Tracer is ONLY absorbed by the lymphatics.
2. Tracer does not aggregate and is well mixed throughout intraperitoneal volume.
3. Tracer label does not dissociate from carrier macromolecules or cells in tissue fluids.
4. Tracer is non-toxic.
5. Tracer is diluted in large enough volume to ensure continuous contact with subdiaphragmatic lymphatics.
6. Low coefficient of variation on repeat measurements under the same experimental conditions.

Table 2. Factors shown to increase peritoneal lymphatic flow rate

1. Raised intraperitoneal hydrostatic pressure.
2. Raised diaphragmatic movement (hyperventilation).
3. Supine posture.
4. After chemical peritonitis.

Factors altering lymphatic absorption

The factors which determine peritoneal cavity lymphatic absorption rate have been studied mainly in animal experiments [28, 39, 41–47]. Both peritoneal transcapillary and lymphatic absorption rates are increased with raised intraperitoneal hydrostatic pressure [28] and are decreased after paracentesis [48]. Lymphatic absorption rate is highly dependent on diaphragmatic movement. Hyperventilation induced by breathing CO_2 increases [41], whereas phrenic neurectomy and anesthesia decrease lymphatic absorption [41, 42]. Upright posture with small intraperitoneal volumes [39] is associated with reduced rates of lymphatic flow although absorption still occurs. Numerous patent diaphragmatic stomata were observed when relaxation of the diaphragm was induced by succinylcholine and when the intraabdominal pressure was raised, whereas few patent stomata were noted when the diaphragm was fixed in contraction by carbachol [43]. It is therefore postulated that suction created by distension of the diaphragmatic lacunae in expiration absorbs peritoneal fluid [44], which is subsequently emptied into the efferent lymphatics during inspiration when the diaphragm contracts and intrathoracic pressure is negative [43, 45]. Valves in the lymphatic ducts maintain forward flow [10, 44] induced by changes in the intrathoracic pressure and by lymphatic contractility. Chemical peritonitis induced by sodium hypochlorite increased the rate of lymphatic absorption in the recovery period [46], perhaps

related to rapid regeneration of end lymphatics after injury [47]. In ascites and peritoneal dialysis the large intraperitoneal volumes ensure continuous contact with the subdiaphragmatic surface and, even when ambulatory, provide conditions for high lymphatic drainage. Factors which increase peritoneal lymphatic flow–rate are summarized in Table 2.

Peritoneal lymphatics in ascites

Although the importance of lymph flow in the pathogenesis of hepatic [22, 49–52] and malignant ascites [34, 35, 53] has been recognized, the role of lymphatic absorption in peritoneal dialysis has been disregarded. In hepatic cirrhosis, peritoneal lymphatic flow increases before ascites develops [49] and ascites only results after overflow of hepatic and intraabdominal regional lymph into the peritoneal cavity (due to increased hepatic sinusoidal and portal hydrostatic pressure and decreased serum oncotic pressure) exceeds peritoneal lymphatic drainage [49–51]. This lymph imbalance accords with both the classic and overflow theories of the pathogenesis of hepatic ascites [54] and is also self–perpetuated by salt and water retention stimulated by a relative decrease in intravascular volume as ascites accumulates. Although lymph flow is increased in hepatic ascites [49, 50, 55], there appears to be an upper limit to the rate of absorption [50, 51, 56]. This is most likely due to progressively increased resistance to lymphatic flow as the absorption rate rises since, although the thoracic duct becomes dilated [55], the ostium of the thoracic duct at the junction of the (L) internal jugular and subclavian veins remains fixed in diameter (56). Cannulation of the thoracic duct resulted in increased lymphatic flow rates in hepatic ascites [55] and in rats infused with intraperitoneal Krebs–Ringer solution [16]. Hepatic ascites has been successfully treated by bypassing this narrowing at the lymphatico-venous junction [57, 58] and by peritoneo-venous shunting [59] which increase the lymphatic flow rate directly and indirectly, respectively. Increased central venous pressure secondary to right heart failure or fluid overload reduces the pressure gradient for lymph flow into the innominate veins [56], and may explain the decreased lymphatic absorption rate that has been reported in nephrogenic ascites [33]. Although the mechanism of increased lymphatic drainage (up to 20 liter/day) in hepatic ascites is not understood, the reduced peritoneal lymphatic absorption observed in malignant ascites [34, 35] is presumed secondary to obstruction of the diaphragmatic lymphatics and draining lymph nodes by metastases [34, 35, 53].

Lymphatic flow rate in peritoneal dialysis

In contrast the contribution of peritoneal lymphatic absorption to net solute mass transfer and ultrafiltration in peritoneal dialysis "ascites" is not well established (Table 3). The mean lymphatic flow rate, determined by the rate of transfer of RISA from peritoneal cavity to plasma, in 10 CAPD patients was 11 · 1 ml/hr (range 4 · 8 to 16 · 6 ml/hr) [60]. However, these results may not be accurate since the elimination rate of RISA from plasma was not included in the calculations, the plasma volumes of these uraemic patients were estimated from their body weight, and the fractional plasma absorption rate was only 20% of the peritoneal disappearance rate. Although this method underestimates peritoneal lymphatic absorption, the above results may be compared with average lymphatic flow rates of 62 ml/hr in hepatic ascites [22], 11 ml/hr in malignant ascites [34] and 15 ml/hr in nephrogenic ascites [33]. Other studies in peritoneal dialysis in man have shown a wide variation in peritoneal transcapillary [61–63] and lymphatic transport [63].

Small increments in hydrostatic pressure in tissues other than the peritoneal cavity increased the lymphatic flow rate until a maximum was reached when tissue pressure was 2 mm Hg above normal [64]. Submesothelial edema is observed in CAPD and may be expected to contribute to increased fluid absorption by interstitial lymphatics in the peritoneal membrane. Raised intraperitoneal volume may increase lymphatic absorption by increasing intraperitoneal hydrostatic pressure and may also explain the elevated peritoneal lymphatic flow rate frequently observed in hepatic ascites [22]. In ascites peritoneal lymphatic absorption rates of greater than 50 ml/hr would be expected unless there were abnormalities in either the diaphragmatic or mediastinal lymphatics [34]. In peritoneal dialysis the rate of decrease of intraperitoneal volume after peak ultrafiltration represents lymphatic absorption in excess of net transcapillary ultrafiltration, and averaged 37 ml/hr in 16 CAPD patients [26]. It would therefore not be unexpected if the daily peritoneal lymphatic flow rate in CAPD "ascites" was greater than 1 liter per day. This accords with the results of our preliminary study of peritoneal lymphatic flow rates in six CAPD patients (unpublished). The lymphatic absorption rate was calculated from the rate of removal of intraperitoneal albumin during an exchange using 2 liter, 2.5% dextrose peritoneal dialysis solution with 30 g added albumin (human serum albumin). The mean lymphatic absorption rate was 85 ml/hr and net (measured) ultrafiltration at the end of the four hour dwell time averaged 329 ml. These results indicate that lymphatic drainage during the four hour dwell reduced the volume of net transcapillary ultrafiltration that could be drained at the end of the exchange by 51%, and thus confirm that ultrafiltration volume is significantly decreased by cumulative lymphatic absorption during the exchange.

However, the delayed effect of CAPD on lymph flow rate remains speculative. If lymphatic absorption increases, solute clearances and observed drainage volume (ultrafiltration) would decrease. These detrimental kinetics are observed in some CAPD patients [61, 62, 65] and are usually attributed to change in the peritoneal membrane, either hyperpermeability, rapid dialysate glucose absorption and early dissipation of the osmotic gradient [62, 66] or sclerosis of the membrane [67–70], rather than elevated lymphatic drainage. Even if lymphatic absorption rate remains unchanged with time on CAPD, it may become relatively more important and clinically significant if the above changes in the peritoneal membrane result in decreased transperitoneal efflux of water and solutes. Net transcapillary ultrafiltration is known to continue in such patients [62, 66], since net ultrafiltration can be observed if the exchange time (and thus cumulative lymphatic drainage) is reduced. Thus, an increase in cumulative lymphatic absorption and/or reduction in cumulative, net transcapillary ultrafiltration (62, 66–70) will result in loss of ultrafiltration. We suspect that ultrafiltration failure occurs when daily lymphatic absorption equals or exceeds daily, net transcapillary ultrafiltration.

Since the mesothelium and endothelium of the diaphragmatic stomata contain actin filaments [44, 71] and the lymphatic ducts have both intrinsic contractility [72] and innervation by non-

Table 3. Transcapillary fluid flux and lymphatic absorption rates in ascites

Ascites	Transcapillary fluid efflux into peritoneal cavity	Peritoneal lymphatic flow rate
Hepatic	+ + +	+ +
Malignant	+	−
Nephrogenic	+	−
Peritoneal dialysis	+ + +	?

Abbreviations are: + increase; − decrease.

myelinated autonomic fibers [73], lymphatic flow rate may be amenable to pharmacological control. Drugs are delivered to lymphatic ducts by the vasa lymphorum [74] as well as lymph, so oral or parenteral medication may alter lymph flow. Although neural blockade by tetrodotoxin had little effect on spontaneous lymphatic contractility [73], inherent myogenicity was decreased by aspirin and indomethacin and increased by leukotrienes and prostaglandin $F_{2\alpha}$ [74]. These latter products of inflammation are found in the dialysate during peritonitis [75] and so loss of ultrafiltration during episodes of peritonitis may be due to increased lymphatic absorption rate as well as enhanced peritoneal membrane permeability and rapid glucose absorption. The contractility of isolated lymphatic vessels was decreased when the calcium antagonist, D-600, was added to the bathing medium [76]. Whether intraperitoneal vasoactive drugs significantly alter lymphatic as well as blood vessel smooth muscle tone and contractility in vivo remains unknown.

Alternative osmotic agents with less transcapillary absorption than glucose have been sought to induce more effective ultrafiltration in peritoneal dialysis [77]. Although macromolecules of molecular weight greater than 19,400 have minimal transcapillary uptake [17], bulk transport via the peritoneal lymphatics means that these macromolecules will still be absorbed, albeit more slowly, and so be potentially toxic systemically. The lymphatic absorption and systemic accumulation of macromolecules, such as gelatins and glucose polymer, have precluded their clinical use as effective osmotic agents. Similarly, any particulate matter [78–80] that is present in the dialysis solution may also be absorbed by the peritoneal lymphatics, although systemic absorption is likely to be less marked than in hemodialysis where direct transfer via the hemodialyzer blood path can occur. Nevertheless this further underlines the importance of minimizing contaminants in commercial peritoneal dialysis solutions.

Bacteria have been observed in thoracic duct lymph in dogs within 10 minutes of intraperitoneal injection [81] and have been recovered in the intrathoracic lymph nodes of patients who have died of peritonitis [82]. Absorption by the peritoneal lymphatics and phagocytosis by resident intraperitoneal macrophages are the major first lines of defence after a bacterial inoculum enters the peritoneal cavity [83], since polymorphonuclear leucocyte influx into the peritoneal cavity is delayed for one to two hours, and sequestration of bacteria by adhesions and fibrin trapping only occurs if infection persists. Consequently thoracic duct ligation reduced bacterial clearance [83], whereas omentectomy had no effect on lymphatic absorption of graphite particles [43]. Despite peritoneal lymphatic absorption, blood cultures during CAPD peritonitis are rarely positive, and pulmonary infections or right sided endocarditis secondary to peritonitis are seldom encountered [84, 85]. It is presumed that the infectious agents are filtered and trapped in the draining lymph nodes. Hence, absorption via the peritoneal lymphatics makes a major contribution to the host defenses of the peritoneal cavity without predisposing the patient on peritoneal dialysis to systemic infections.

Although the physiological role of the lymphatics in improving host defences and maintaining a small volume of isosmotic fluid in the peritoneal cavity is presumably beneficial, ultrafiltration and solute kinetics in peritoneal dialysis may be influenced adversely by peritoneal cavity lymphatic absorption. Since lymphatic drainage in peritoneal dialysis has been underinvestigated, further studies are needed to determine if cumulative lymphatic absorption during the dwell time significantly reduces net ultrafiltration volumes and solute clearances.

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