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Flow and Composition of Renal Hilar Lymph During Volume Expansion and Saline Diuresis

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Summary

Volume expansion of 5–10 % body weight in dogs was achieved by infusion of 0.9 %, 1.2 % or 0.4 % saline. The average diuretic response for each group was 9.9 ± 2.1, 5.5 ± 0.6 and 3.3 ± 0.9 (mean ± S.E.) ml/hr/kg respectively. Flow from single hilar lymphatics increased by an average of 150 %, there being no significant difference between the groups. A significant ($p < 0.02$) positive correlation was found between the increase in hilar lymph flow and thoracic duct lymph flow. No correlation was found between hilar lymph flow and the extent of the diuresis. Control hilar lymph contained higher concentrations of Na^+ (L/P = 1.05) and Cl^- (L/P = 1.12) ($P < 0.001$) and lower concentrations of glucose (L/P = 0.86) ($p < 0.001$) than did simultaneous plasma. The electrolyte lymph-to-plasma differences were maintained despite increases or decreases in plasma concentrations. The results indicate that changes in hilar lymph flow are related to volume expansion rather than to the diuresis, and that the processes responsible for lymph-to-plasma compositional differences are relatively unaffected by changes in plasma levels.

Water diuresis, when induced by hypotonic volume expansion of 5 to 10 % body weight in the dog, increases renal lymph flow by a mean value of 125 % (1). The hypotonic infusion also lowers both plasma and renal lymph electrolyte levels but fails to alter the relative differences between the two which are found under control conditions. For Na^+ and Cl^-, control hilar lymph-to-plasma ratios have a mean value of approximately 1.050 and 1.130 respectively (1, 2, 3), and therefore cannot be accounted for by the Gibbs-Donnan phenomenon. These observations demonstrate that the process responsible for the comparatively higher concentrations of Na^+ and Cl^- in hilar lymph is relatively unaffected by the diuresis. The reverse situation exists during furosemide diuresis where renal lymph flow is relatively unaffected, that is unless renal blood flow increases markedly (4, 5). Furosemide also reduces or abolishes the electrolyte differences between lymph and plasma. The latter finding has been interpreted as physiological evidence for an outer medullary component to renal hilar lymph (5).

The present study was primarily concerned with the effects of saline diuresis, induced by isotonic and hypertonic volume expansion, upon the flow and composition of renal lymph. It was found that renal hilar and thoracic duct lymph flow were increased in a comparable manner to that found in hypotonic infusion and that electrolyte differences between renal lymph and plasma were maintained in the face of rising plasma concentrations.

Materials and Methods

The experiments were carried out on dogs of either sex with an average weight of 18 kg. Fifteen animals were anesthetized with sodium pentobarbital (25–30 mg/kg body wt) and three with 1 % chloralose (Kuhlman, Paris, France) (initial dose 170 mg/kg; sustaining dose 35 mg/kg/hr approximately).

The experimental protocol was similar to that described previously for hypotonic volume expansion (1). Plasma samples were obtained at 30 minute intervals from the carotid artery and renal vein; the latter being cannulated through the gonadal vein. Thoracic duct lymph was drained continuously from a cannula inserted in the neck, and at 30 minute intervals a sample was retained for analysis and the remainder injected intravenously. On the left side, the ureter and one hilar lymphatic were cannulated through a loin incision.

Volume expansion of 5–10 % body weight was obtained by infusion of isotonic saline (0.9 %) in seven animals and hypertonic saline

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(1.2 %) in another seven. In the hypertonic group, four were anesthetized with sodium pentobarbital and three with chloralose. The reason for the latter was to ensure that chloralose, which had been used as the anesthetic in a previous study on water diuresis (1), did not have a specific effect upon lymph formation. In addition four dogs, anesthetized with sodium pentobarbital, were infused with hypotonic (0.4 %) saline amounting to 10 % of body weight.

Prior to volume expansion each animal served as its own control for approximately two hours, during which isotonic saline was infused at about 1 ml/min. The appropriate saline was then infused either rapidly, over a 90 minute period, or by a series of injections each of up to 500 ml in volume. Additional saline, equivalent to urine loss was also injected. Urine and lymph samples were collected more frequently during volume expansion than during control periods because of the higher rates of flow.

The Student t test for paired groups was used to estimate significance. The means of the concentrations and ratios were calculated for each experiment, and the statistical tests were then applied to the overall sets of means.

Samples were analyzed for Na^+ and K^+ with an IL 343 automatic readout flame photometer having a built in dilutor, and for Cl^- with a Corning model 920 M meter. Glucose was measured by the routine ortho-toluidine in glacial acetic acid technique; blood urea nitrogen by the diacetyl monoxime method using Harleco blood urea nitrogen sets; and protein concentrations were read on an AO refractometer. All optical densities were obtained using a Coleman 55 spectrophotometer.

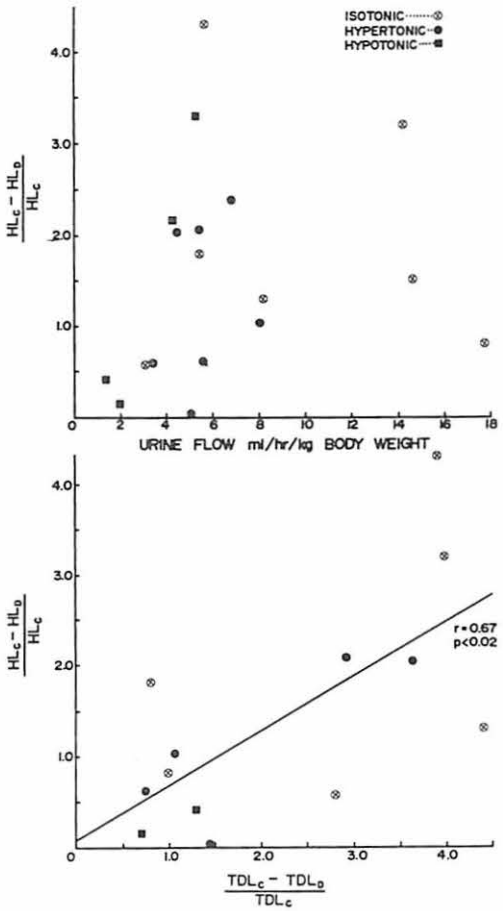

Figure 1 The lower part of the figure demonstrates the correlation between the increase in hilar lymph flow (HL) and thoracic duct lymph flow (TDL) during volume expansion. The upper part of the figure shows the lack of correlation between the hilar lymph flow increase and the extent of the diuresis.
Subscripts C = control, D = during diuresis.

Results

Lymph Flow. Thoracic duct and single hilar lymphatic flow for control periods in all experiments were 2.2 ± 0.19 and 0.086 ± 0.02 (mean ± S.E.) ml/hr/kg body weight respectively. Volume expansion, as expected, increased both values significantly ($p < 0.01$). Although the extent of the increase varied considerably from one experiment to another, the average values for the different groups were relatively comparable. Thus the respective percentage increases for hilar and thoracic duct lymph flow during isotonic, hypertonic and hypotonic expansion were 194, 124, 150 (HL) and 281, 196 and 91 (TDL). Figure 1 shows how the increases in individual experiments correlated with one another ($r = 0.67$, $p < 0.02$), as well as the correlation between the extent of the diuresis and the increase in hilar lymph flow ($r = 0.2$, n.s.).

Table 1 Control values obtained in all 18 experiments for arterial plasma (AP), renal venous plasma (RVP), hilar lymph (HL) and thoracic duct lymph (TDL).

		Na^+ mEq/L	Cl^- mEq/L	K^+ mEq/L	Glucose mgm/100 ml	Urea mgm/100 ml	Protein gm/100 ml
AP	$\overline{X}$	145.3	113.7	3.6	94.2	16.1	5.5
	S.E.	0.7	1.0	0.07	3.2	1.0	0.12
(n = 18)							
RVP	$\overline{X}$	145.4	113.4	3.5	95.1	14.8	5.5
	S.E.	0.7	0.9	0.07	2.8	0.8	0.12
(n = 18)							
HL	$\overline{X}$	153.2*	127.3*	3.8*	81.7*	15.7	2.1*
	S.E.	1.0	1.4	0.07	3.0	1.05	0.14
(n = 18)							
TDL	$\overline{X}$	146.2	115.2	3.7	92.7	15.2	3.7*
	S.E.	0.7	0.8	0.1	2.7	1.2	0.19
(n = 13)							

* Significantly different from RVP $p < 0.001$.

Composition. The average control values for all experiments are shown in Table 1, there being no difference between the three groups. With the exception of K^+ ($p < 0.001$) and urea ($p < 0.001$) there was no significant difference between renal venous and arterial plasma. Nor, apart from protein, was there a difference between thoracic duct lymph and either arterial or venous plasma. Hilar lymph, on the other hand contained significantly greater concentrations of Na^+, Cl^-, and K^+, and lower concentrations of glucose and protein than plasma or thoracic duct lymph. The urea concentration of hilar lymph lay between the values for arterial and venous plasma, but the differences were not statistically significant.

The effect of volume expansion on Na^+, Cl^- and protein concentrations in plasma and hilar lymph is shown in Figure 2. Isotonic fluid had little or no effect upon Na^+ concentration in both lymph and plasma. Hypertonic and hypotonic fluid increased and decreased, respectively, the Na^+ and Cl^- concentrations of both plasma and lymph such that the lymph-to-plasma differences remained statistically significant at the $P < 0.01$ or $P < 0.001$ levels. The reduction in protein concentrations was comparable in the three groups.

Glucose and urea concentrations in both lymph and plasma were reduced during the height of the infusion, but in the majority of experiments returned to control levels within an hour. The hilar lymph-to-plasma ratio for glucose remained significantly below one regardless of the drop in plasma glucose.

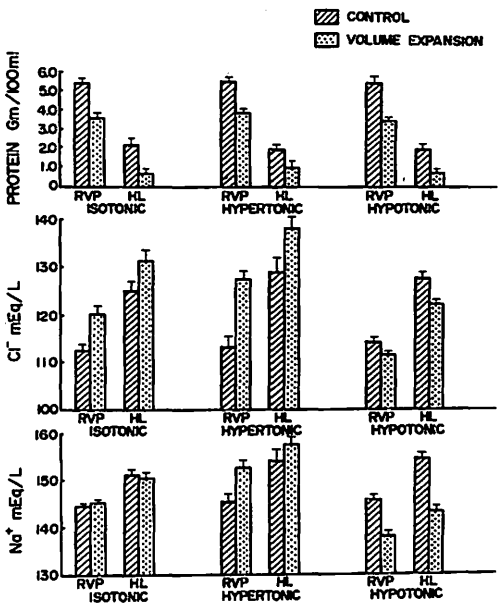

Figure 2 The effect of volume expansion on plasma and lymph Na^+, Cl^- and protein concentrations is shown. The lymph to plasma Na^+ and Cl^- differences were maintained in spite of concentration increases and decreases. Arterial plasma and thoracic duct lymph Na^+ and Cl^- levels are not shown because they mimicked renal venous plasma (RVP).
Hilar lymph = HL.

Discussion

The association between diuresis and an increase in renal lymph flow has been known for many years (6). However, the importance attached to this association has been misleading since there is little or no evidence that the diuresis *per se* affects the rate of lymph formation. On the contrary, the evidence suggests that associated conditions, especially the volume expansion and change in renal blood flow, are the determining factors. Thus furosemide, in the absence of volume expansion does not increase lymph formation by the kidney unless the concomitant increase in renal blood flow is marked (4, 5). Similarly the rise in lymph flow which accompanies mannitol diuresis (5) can be explained by the volume expansion, by its osmotic effect in interstitial fluid and lymph, and by the increase in renal blood flow which accompanies its administration. The results of the study reported here are consistent with this general concept. For example, the extent of the percentage increase in renal lymph flow corresponded to the generalized effect on lymph formation, as observed in the thoracic duct, and there was a significant positive correlation between the two (Figure 1). No correlation, on the other hand, was found to exist between the increase in renal lymph flow and the extent of the diuresis (Figure 1). The changes in lymph flow could therefore be attributed to the associated volume expansion rather than to the diuresis induced. In addition the mean diuresis (3.24 ± 0.92 S.E., ml/hr/kg body weight) obtained during hypotonic volume expansion in the present study was significantly less than that obtained in a previous study (12.4 ± 2.6), yet the percentage increase in hilar lymph flow was comparable (150 % and 125 % respectively) (1). The volume expansion was similar in both experiments and the diuretic difference was attributable to the chloralose anesthesia used in the earlier study. In contrast to the diuretic response, chloralose was not found to have any specific effect upon renal lymph flow. Although para-amino hippurate and inulin were infused and monitored in both studies, the variation in lymph flow between animals was such as to preclude any conclusion on changes induced by altered renal blood flow during volume expansion and diuresis.

The comparative composition of plasma and lymph under control conditions as seen in Table 1 were similar to those obtained in earlier studies (2, 5). Hilar lymph contained a significantly lower concentration of glucose than did plasma (L/P = 0.85), and this has been attributed to a component derived from glucose-free tubular fluid reabsorbed distal to the proximal convoluted tubule (2). Although glucose concentrations were temporarily reduced by the infusion fluid the lymph-to-plasma difference was relatively unaffected. Na^+ and Cl^- on the other hand have higher concentrations in hilar lymph than plasma. Current evidence (5, 7) indicates that the levels of these electrolytes in hilar lymph are in part a reflection of the outer medullary interstitial fluid, which is affected by the electrolyte pump in the ascending thick limb of Henle. In the presence of this pump Cl^- and Na^+ enter the interstitium without an osmotically equivalent volume of fluid. Inhibition of the pump leads to isosmotic interstitial fluid, and the electrolyte content of hilar lymph falls (5). The present study is consistent with this interpretation, since the lymph-to-plasma ratio for Na^+ and Cl^- was maintained in spite of significant increases or decreases in the plasma concentrations. Such a finding would be expected if, as has been shown (8, 9), electrolyte transport by the thick ascending limb of Henle is not abolished by volume expansion.

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