JCI The Journal of Clinical Investigation

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J Clin Invest. 1962;41(11):1971-1980. https://doi.org/10.1172/JCI104655.

Research Article

Journal of Clinical Investigation
Vol. 41, No. 11, 1962

THE USE OF LYMPH FOR THE MEASUREMENT OF GAS TENSIONS IN INTERSTITIAL FLUID AND TISSUES *

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(Submitted for publication April 26, 1962; accepted July 12, 1962)

The concentrations of the respiratory gases in tissues are interesting for several reasons: *1*) as an index of the relationship between the oxidative metabolism of the tissue and its blood supply, *2*) as a measure of the gas tensions under which the metabolic processes of the different tissues operate, and *3*) for the understanding of the interplay between external respiration, blood, and internal respiration.

Previous attempts to measure gas tensions of tissues have involved the analyses of the gaseous composition of body fluids (1–3), the sampling of gas from artificial pockets created within tissues (4–8), and the direct implantation of polarographic electrodes (9–11). Unfortunately, results obtained by such methods are apt to be unreliable because of artefacts incident to the introduction of electrodes into tissues, the lack of dependable instruments for the precise measurement of the small quantities of oxygen in biological fluids, and the inability to calibrate electrodes implanted in tissues.

The present study was designed to circumvent some of these difficulties by substituting lymph for tissues (12). This approach to the composition of gases in tissues presupposes that interstitial fluid equilibrates with the tissues which it bathes before it enters the lymphatic capillaries and that it undergoes insignificant changes in its gaseous composition as it courses along the lymphatic tree. It has the advantage of avoiding trauma to tissues and blood vessels and of providing a fluid which can be precisely analyzed for oxygen and carbon dioxide tensions.

* This investigation was supported in part by a research grant from the National Heart Institute, U. S. Public Health Service Grant H-2299 (C), with additional support from the American Heart Association and the New York Heart Association.

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METHODS

Thirty-three dogs were operated upon, but the data in this paper refer only to the twenty-one animals in which the cervical portion of the thoracic duct was successfully isolated for anaerobic sampling. All studies were performed approximately twelve hours postprandially, under general anesthesia induced with intravenous Nembutal (30 mg per kg of body weight). The femoral artery and vein were exposed, an indwelling arterial needle was inserted, and a single lumen catheter was introduced into the femoral vein and placed under fluoroscopic control so that its tip lay in the inferior vena cava immediately below the right atrium. The inferior vena cava was chosen as the source of blood for comparison with lymph because its blood drains those organs and tissues that contribute the major share of lymph to the thoracic duct (13).

The isolation of the cervical portion of the thoracic duct involved the careful dissection of the external jugular vein to its junction with the axillary and subclavian veins. In seven of the dogs, the thoracic duct could be identified as a distinct vessel; in these animals, the duct was cannulated with polyethylene tubing and the tubing was sewn into place to provide an air-tight source of lymph. In the remaining dogs, the thoracic duct seemed to consist only of many small branches; in these animals, the subclavian venous segment into which these branches drained was isolated from the rest of the venous system by ligatures and the small venous pocket thus created was cannulated as the source of thoracic duct lymph. Finally, the trachea of each dog was intubated with a cuffed endotracheal tube which led, in turn, to a Starling pump.

In eight of the twenty-one dogs, the O_2 and CO_2 tensions of lymph were compared with those of arterial and venous blood at different levels of alveolar ventilation. For this purpose, each animal was ventilated at two or three different levels of minute ventilation. Each level of ventilation was continued for approximately 45 minutes; at the end of this period, samples of lymph and of arterial and venous blood were drawn simultaneously under anaerobic precautions.

In four other dogs, the concentrations of lactate in lymph were compared with the corresponding concentrations of lactate in arterial and venous blood. In each dog, lymph and blood were sampled from different regions: in dogs 9 and 10, from the cervical thoracic duct and the inferior vena cava at its juncture with the

atrium; in dog 11, from the cysterna chyli and the inferior vena cava below the entrance of the hepatic veins; and in dog 12, from the cervical duct and the external jugular vein.

The remaining experiments were designed to determine the extent to which the gaseous composition of lymph was altered by the metabolic activity of *1)* the lymphocytes contained in lymph, *2)* the walls of the lymphatic vessels, and *3)* the lymph nodes through which the lymph passes.

As a measure of the metabolic activity of the cellular elements of the lymph, the oxygen consumption of lymph was measured *in vitro:* thoracic lymph from three dogs was exposed to a gas mixture of known oxygen and carbon dioxide tension; a continuous-flow, open-tonometric system was used for the equilibration. At the end of an hour of equilibration, the lymph was withdrawn anaerobically from the tonometers. Thereafter, the rate of change in the oxygen tensions of each sample was measured polarographically at ten- to fifteen-minute intervals for the ensuing one to two hours.

As an index to the influence of the lymphatic walls on the gas tensions of the lymph, not only the thoracic duct, but also one other lymph channel were cannulated in four other dogs—either the femoral duct in the groin (two dogs), the cysterna chyli (one dog), or the cervical duct high in the neck (one dog). In these animals, the gaseous composition of simultaneously drawn, regional lymph and blood were compared—femoral duct lymph with femoral venous blood, cysterna chyli lymph with blood drawn from the inferior vena cava below the entry of the hepatic veins, and cervical lymph with external jugular venous blood. Lymph from each of these sampling sites was also compared with simultaneously drawn samples from the thoracic duct.

Finally, as a device to deplete the lymph nodes of lymphocytes and thereby diminish the metabolic activity of the lymph nodes through which lymph passes en route to the thoracic duct, five dogs were treated with prednisolone-21-phosphate, 10 mg per kg of body weight, by intramuscular injection daily for 6 to 8 days prior to the cannulation of the thoracic duct. The samples of blood and lymph from these animals were analyzed for oxygen tension and cellular content.

Samples of lymph from four of the first eight dogs were used for the determination of the apparent dissociation constant of carbonic acid in lymph.

Analytic techniques. The oxygen tensions (P_{O_2}) of blood and lymph were measured by a modified Clark needle electrode (14–16). The tip of the electrode was covered with a polyethylene membrane so that a 30 per cent solution of potassium chloride was contained between the tip and the membrane. The needle electrode was housed in a glass cuvette in such a way that samples and calibrating solutions could be drawn over the tip of the electrode. The cuvette was immersed in a constant temperature water bath at 37.5° C. The solutions for the calibration of the polarograph were prepared by tonometric equilibration of 0.8 per cent saline with gases of known oxygen tensions. Before and after analysis of each unknown sample, the polarograph was calibrated with at least four solutions of different O_2 tensions, ranging from 0 to 90 mm Hg. Both the samples and the calibrating solutions were passed through the cuvette at the same rate, i.e., 4 ml per minute. Duplicate measurements of each sample were required to check to within 1 mm Hg at oxygen tensions of 18 to 100 mm Hg and within 2.5 mm Hg at oxygen tensions of 0 to 18 mm Hg.

The oxygen saturation (S_{O_2}) of blood and the carbon dioxide content (C_{CO_2}) of blood and lymph were measured by the manometric technique of Van Slyke and Neill (17). The pH of blood and lymph was determined with the McInnes-Belcher glass electrode at 37.5° C. The carbon dioxide tension (P_{CO_2}) of blood was derived from the pH and C_{CO_2} of whole blood by using the line charts of Van Slyke and Sendroy (18). The P_{CO_2} of lymph was obtained from the pH and C_{CO_2} by using the Henderson-Hasselbalch relationship. To apply this equation to lymph, the negative logarithm of the apparent dissociation constant (pK_a) was determined by *1)* equilibrating lymph for one hour with a gas mixture of a known P_{CO_2}, *2)* determining the pH and C_{CO_2} of the lymph at the conclusion of the equilibration, and *3)* solving the Henderson-Hasselbalch equation for the unknown pK_a by using the known P_{CO_2} and the measured pH and C_{CO_2} of lymph.

The concentrations of lactate in blood and lymph were determined by the method of Barker and Summerson (19). Protein- and sugar-free filtrates of the samples were made at identical times after withdrawal, i.e., within ten minutes. For the sake of comparison, the concentrations of lactate in blood and lymph are expressed in terms of the water content of the blood and lymph (20). The water content of the samples was determined by measuring the changes in weight of samples of known volume after dessication at 24° C for 48 hours.

RESULTS

The data used for the calculation of the pK_a of lymph appear in Table I. The average of the calculated values for pK_a is 6.08, with a range of $\pm$ .03.

Table II compares the composition of lymph and blood with respect to pH and to oxygen and

TABLE I

The pK_a of lymph

Dog	Imposed P_{CO_2}	Measured pH	Measured C_{CO_2}	Calculated pK_a
	mm Hg		*ml/100 ml*	
1	35	7.13	27.0	6.06
2	72	7.08	49.4	6.11
3	30	7.40	42.1	6.09
4	35	7.30	42.0	6.07

TABLE II

The composition of lymph and blood at different levels of minute ventilation in the dog *

Dog	$\dot{V}_E$	Source	pH	Cs_{CO_2}	P_{CO_2}	C_{bO_2}	S_{O_2}	P_{O_2}	Q_l
	L/min/kg			*ml/100 ml*	*mm Hg*	*ml/100 ml*	*%*	*mm Hg*	*ml/min*
1		Art	7.32	56.8	47	17.2	94	86	
15.1 kg	.157	IVC	7.30	57.7	51	13.9	66	44	1.4
		Lymph	7.26	60.0	57			8	
		Art	7.34	52.2	44	17.1	92	88	
	.192	IVC	7.32	56.6	46	12.4	67	46	1.4
		Lymph	7.28	57.1	52			12	
		Art	7.47	42.6	26	17.9	94	90	
	.295	IVC	7.45	49.1	31	12.2	61	37	1.6
		Lymph	7.38	49.8	37			10	
2		Art	7.33	54.8	45	16.7	86	67	
16.0 kg	.190	IVC	7.31	55.8	58	13.0	63	41	2.4
		Lymph	7.26	56.4	55			7	
		Art	7.41	43.9	30	14.2	88	74	
	.250	IVC	7.39	48.0	35	11.1	63	40	2.0
		Lymph	7.32	49.0	40			8	
		Art	7.47	36.1	22	15.8	92	77	
	.300	IVC	7.45	39.0	25	12.7	72	38	1.6
		Lymph	7.40	39.9	29			3	
3		Art	7.31	54.6	47	15.6	94	83	
15.4 kg	.100	IVC	7.28	55.6	51	13.4	77	48	0.8
		Lymph	7.26	55.6	53			5	
		Art	7.34	49.4	39	15.8	94	86	
	.190	IVC	7.30	51.4	45	12.8	76	50	1.1
		Lymph	7.28	51.3	49			12	
		Art	7.41	37.2	27	15.2	95	92	
	.340	IVC	7.37	39.0	31	12.4	77	51	1.1
		Lymph	7.34	39.4	36			8	
4		Art	7.32	55.5	50	19.3	95	92	
14.2 kg	.097	IVC	7.28	56.7	55	15.6	76	51	2.8
		Lymph	7.22	57.2	59			6	
		Art	7.34	45.8	44	18.6	96	90	
	.210	IVC	7.32	56.8	49	13.9	72	42	2.0
		Lymph	7.27	56.6	55			12	
		Art	7.40	45.6	33	18.8	95	91	
	.300	IVC	7.35	48.3	38	14.2	72	44	2.4
		Lymph	7.29	51.0	46			14	
5		Art	7.35	54.5	43	18.9	94	83	
10.6 kg	.085	IVC	7.32	56.8	47	14.7	73	41	1.8
		Lymph	7.26	57.0	55			6	
		Art	7.50	35.3	20	18.0	95	90	
	.310	IVC	7.46	39.6	25	14.4	76	42	1.8
		Lymph	7.40	41.1	32			8	
6		Art	7.36	50.9	39	18.1	96	77	
12.0 kg	.209	IVC	7.35	52.8	42	14.3	76	42	2.4
		Lymph	7.33	55.0	46			13	
		Art	7.45	42.0	27	18.3	96	79	
	.250	IVC	7.41	47.2	33	15.4	76	41	2.6
		Lymph	7.35	49.1	38			12	

* Symbols: $\dot{V}_E$ = minute ventilation; Cs_{CO_2} = CO_2 content of serum or lymph [values for blood were derived from the line charts of Van Slyke and Sendroy (18)]; P_{CO_2} = carbon dioxide tension of blood or lymph; C_{bO_2} = oxygen content of blood; S_{O_2} = oxyhemoglobin saturation of blood; P_{O_2} = the oxygen tension of blood or lymph; $\dot{Q}_l$ = the rate of flow of lymph from the cannulated thoracic duct.

TABLE II—(*Continued*)

Dog	$\dot{V}_E$	Source	pH	C_{SCO_2}	P_{CO_2}	C_{bO_2}	S_{O_2}	P_{O_2}	$\dot{Q}_l$
	L/min/kg			*ml/100 ml*	*mm Hg*	*ml/100 ml*	%	*mm Hg*	*ml/min*
7		Art	7.36	55.8	43	19.0	97	100	
18.2 kg	.135	IVC	7.34	56.8	45	14.8	76	43	1.4
		Lymph	7.30	58.0	51			4	
		Art	7.41	51.0	35	19.5	97	100	
	.274	IVC	7.38	54.5	41	15.7	78	44	2.0
		Lymph	7.33	56.0	47			10	
3		Art	7.36	49.6	37	16.0	98	90	
13.0 kg	.130	IVC	7.35	51.7	41	11.9	81	43	1.8
		Lymph	7.30	54.3	48			9	
		Art	7.41	47.4	31	16.1	99	94	
	.258	IVC	7.38	48.2	38	12.0	81	45	1.6
		Lymph	7.35	49.6	41			9	

carbon dioxide contents and tensions. For each animal, the initial level of minute ventilation was set to duplicate the predicted ventilation at rest (21). At these levels of minute ventilation, lymph had a lower pH and a higher CO_2 content (C_{CO_2}) and tension (P_{CO_2}) than did arterial or venous blood. As may be seen in Figure 1, the differences between the P_{CO_2} of lymph and blood were small: the P_{CO_2} of lymph averaged 5 ± 3 mm Hg higher than the P_{CO_2} of venous blood and 8 ± 3 mm Hg higher than the P_{CO_2} of arterial blood. On the other hand, the oxygen tension (P_{O_2}) of lymph differed markedly from the P_{O_2} of blood; whereas the average P_{O_2} of arterial blood was 80 mm Hg and that of venous blood 42 mm Hg, the P_{O_2} of lymph averaged only 8 ± 6 mm Hg.

The effects of increasing the minute ventilation

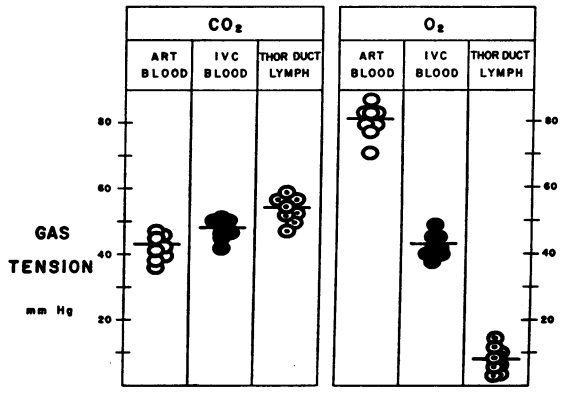

FIG. 1. THE O_2 AND CO_2 TENSIONS OF THORACIC DUCT LYMPH, ARTERIAL BLOOD, AND BLOOD FROM THE INFERIOR VENA CAVA DRAWN SIMULTANEOUSLY FROM EIGHT DOGS AFTER 45 MINUTES OF CONSTANT MINUTE VENTILATION.

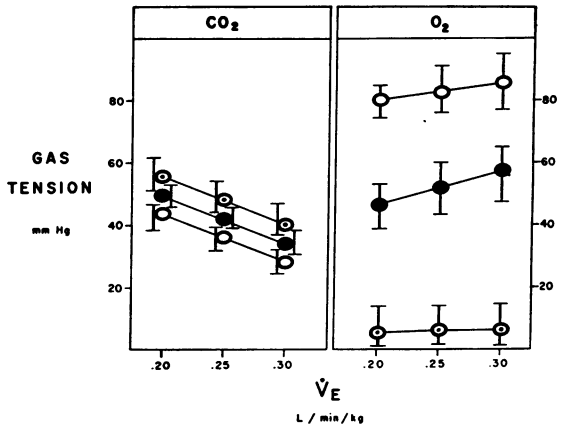

FIG. 2. THE AVERAGE O_2 AND CO_2 TENSIONS OF THORACIC DUCT LYMPH, ARTERIAL BLOOD, AND BLOOD FROM THE INFERIOR VENA CAVA FROM EIGHT DOGS AT DIFFERENT LEVELS OF MINUTE VENTILATION ($\dot{V}_E$). Each level was maintained for 45 minutes prior to sampling. Open circles = arterial blood; solid circles = venous blood; bull's-eyes = lymph.

on the gaseous composition of lymph and blood are listed in Table II. Despite general anesthesia, the arteriovenous differences in oxygen content were normal at the initial level of minute ventilation; moreover, neither the arteriovenous differences in oxygen content nor the rate of lymph flow were appreciably effected by the augmented ventilation. As may be seen in the individual data of this table and in the schematic representation of average values in Figure 2, the C_{CO_2} and P_{CO_2} of lymph and of arterial and venous blood all decreased in a parallel fashion during the periods of augmented ventilation. By way of contrast, even

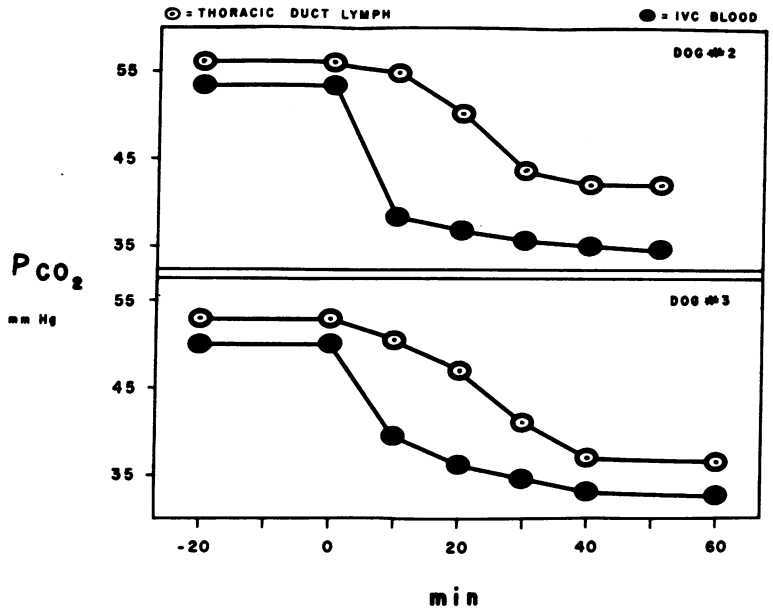

FIG. 3. THE RATE OF CHANGE IN THE P_{CO_2} OF LYMPH AND BLOOD FROM THE INFERIOR VENA CAVA IN TWO DOGS AFTER AN ARTIFICIAL INCREASE IN MINUTE VENTILATION. Time 0 and time −20 represent control values, and subsequent times represent values during augmented ventilation. Solid circles = venous blood; bull's-eyes = lymph.

though the arterial P_{O_2} increased during the periods of augmented ventilation, the P_{O_2} of lymph remained virtually unchanged from the initial period.

The prospect that these values for gaseous composition reflect an unsteady state of respiratory gas exchange between lymph and blood is analyzed in Figure 3. This figure compares the P_{CO_2} of samples of lymph and inferior vena caval blood drawn at 15-minute intervals from two dogs during the hour following an abrupt increment in minute ventilation. Although the two dogs were of approximately the same weight, their rates of lymph flow were somewhat different, i.e., 1.8 and 2.4 ml per minute, respectively. It is apparent that the changes in the P_{CO_2} of venous blood resulting from the augmented ventilation were virtually complete by 10 to 15 minutes; on the other

TABLE III

The concentrations of lactate in lymph and blood *

Dog	Lactate		
	Arterial	Venous	Lymph
	mg/100 ml H_2O		
9	19.2	21.0	24.5
		21.0	24.0
10	18.0	20.5	25.0
11	20.5		27.5
			27.0
12	13.0	14.0	19.0

* Sources of samples: *1*) venous: dogs 9 and 10, inferior vena cava at its junction with the atrium; dog 11, the inferior vena cava below the entrance of the hepatic veins; dog 12, the external jugular vein; *2*) lymphatic: dogs 9 and 10, the thoracic duct in the neck; dog 11, the cysterna chyli; dog 12, the cervical duct.

TABLE IV

The O_2 consumption of lymph

Dog	Original P_{O_2} of lymph	Time elapsed	Consecutive P_{O_2} of lymph
	mm Hg	*min*	*mm Hg*
1	69	0	69
		15	70
		60	67
2	146	0	145
		15	141
		30	141
		60	142
		90	141
3	67	0	67
		30	64
		60	61
		80	61

hand, approximately 40 minutes was required to achieve stable P_{CO_2} values in lymph. Despite the variations in the rate of lymph flow, this figure also indicates that the initial difference between the P_{CO_2} of lymph and blood, the time of the first change in the P_{CO_2} of lymph after the beginning of augmented ventilation, and the time for the achievement of stable P_{CO_2} values were virtually the same in the two animals.

In Table III, the concentrations of lactate in lymph and blood are compared. Despite the different sites from which the lymph was sampled, the lactate levels of lymph uniformly exceeded that of the corresponding regional venous blood by approximately 15 to 20 per cent.

The prospect that lymphocytes or other constituents of lymph may consume some of the oxygen carried in lymph is analyzed in Table IV. The initial P_{O_2} of lymph (time 0) was determined polarographically immediately after the tonometric equilibration of lymph with gases of known oxygen compositioin. After 1 to 1½ hours, repeated polarographic measurements indicated only a slight decrement in the lymph P_{O_2} (2 to 6 mm Hg).

Data relevant to the prospect that the lymphatic vessels may consume some of the oxygen carried in the lymph appear in Table V. This table compares the P_{O_2} of lymph drawn from two distant parts of the lymphatic tree in each of four animals. It may be seen that the P_{O_2} of each set of samples is virtually identical, i.e., the P_{O_2} of lymph from the femoral duct, the high cervical region, or the cysterna chyli undergoes no change during its slow transit to the thoracic duct in the neck.

TABLE V

Comparison of the P_{O_2} of regional lymph and venous blood

Dog	Lymph source	Venous blood source	Lymph P_{O_2}	Venous P_{O_2}
			mm Hg	*mm Hg*
13	Cervical duct	Ext. jugular	7	22
	Thoracic duct	Inf. vena cava	8	41
14	Femoral duct	Femoral	12	26
	Thoracic duct	Inf. vena cava	13	40
15	Cysterna chyli		6	
	Thoracic duct		6	
16	Femoral duct	Femoral	5	30
	Thoracic duct	Inf. vena cava	6	42

TABLE VI

The P_{O_2} of lymph from dogs treated with prednisolone

Dog	Lymph P_{O_2}	Venous P_{O_2}	Lymphocytes in lymph
	mm Hg	*mm Hg*	*cells/mm³*
17	17	50	85
18	4	33	40
19	15	28	10
20	4	34	20
21	11	37	30

In Table VI are listed the O_2 tensions of lymph after prednisolone treatment. In these five animals, the average lymphocyte count is 37 per mm³ of lymph as compared to the average value of 650 lymphocytes per mm³ of lymph obtained from the thoracic duct of ten untreated animals. Despite this difference in cellularity, the average O_2 tension of lymph in the treated animals is similar to that of the untreated animals (10 mm Hg).

DISCUSSION

The present study revealed that marked differences exist between the gaseous composition of lymph and blood: the P_{CO_2} of lymph was invariably higher than the P_{CO_2} of venous blood; the P_{O_2} of lymph was not only lower than that of venous blood but averaged only 8 mm Hg. If we assume that the gas tensions of lymph mirror the gas tensions of some portion of the tissues with which lymph comes into contact, these results suggest that some tissues normally operate at mean O_2 tensions considerably lower than those generally accepted on the basis of values derived from venous blood (4, 11). Although these low O_2 tensions are still consistent with an aerobic form of metabolism in the bulk of tissues, the high lactate levels in lymph suggest that some portions of the tissues, at least intermittently, metabolize in an anaerobic environment.

Critique of the present study

There are two major alternatives to the idea that the gas tensions of lymph represent the gas tensions of the peripheral tissues from which the lymph was derived: *1*) an unsteady state of gas exchange, and *2*) the metabolic activity of the lymphocytes carried by lymph, of the lymphatic vascular walls, and of the lymph nodes.

1. The steady state of gas exchange. It is well known that the blood P_{CO_2} rapidly responds to a change in alveolar ventilation. On the other hand, it seems likely that the P_{CO_2} of lymph would respond more slowly to changes in alveolar ventilation. This delay would be expected to arise not only from the time required for the gas tensions of the interstitial fluid to equilibrate with blood, but also from the transit time (10 to 15 minutes) required for lymph to pass from the tissues to the thoracic duct (*22*). The present study confirmed that an acute change in the level of ventilation was associated with only gradual changes in the P_{CO_2} of lymph. Consequently, the P_{CO_2} gradient between blood and lymph during augmented ventilation can only become meaningful for stable physiologic conditions when sufficient time is allowed for a new steady state to occur. As a corollary, failure to allow sufficient time for a new equilibrium between blood and lymph may cause extraordinary P_{CO_2} gradients between blood and lymph; such inordinate P_{CO_2} gradients (10 to 25 mm Hg) have been reported by others (*23*). However, large gradients for P_{CO_2} between blood and interstitial fluid in a steady state are unlikely because of the great solubility of CO_2.

In contrast to the marked effect on blood P_{CO_2}, augmented ventilation has little influence on the oxygen content of systemic arterial blood, i.e., the blood delivered to the systemic capillaries, since the hemoglobin of this blood is almost fully saturated during eupnea. Since the cardiac output and the metabolic rate are also generally unaffected by hyperventilation (*24*), there is no reason to expect a change in the tissue P_{O_2}. In keeping with these considerations and the idea that lymph provides a measure of tissue P_{O_2} are the data of the present study, which demonstrated that alveolar hyperventilation failed to affect the P_{O_2} of lymph.

2. Metabolic activity of the lymphocytes carried by the lymph, of the lymphatic vascular walls, and of the lymph nodes. Once the interstitial fluid has entered the lymphatic capillaries and begun its journey as lymph to the large ducts from which it can be sampled, its P_{O_2} may conceivably be decreased and its P_{CO_2} increased by the metabolic activity of three types of cells or tissues: *1*) the lymphocytes contained in the lymph, *2*) the walls of the lymphatic vessels, and *3*) the lymph nodes.

The first possibility seems unlikely unless the metabolic activity of the lymphocyte *in vivo* differs markedly from that *in vitro*. The metabolic activity of the lymphocytes *in vitro* does not appear able to account for a sizeable P_{O_2} gradient between lymph and venous blood, since the rate of fall in the P_{O_2} of separated lymph was found to be slow (*2* to 6 mm Hg per hour).

Nor did the present study provide evidence in support of the second possibility. The metabolic activity of the walls of the thoracic duct was not responsible for the low P_{O_2} values of lymph, since virtually identical O_2 tensions were found in lymph samples obtained from the central and peripheral portions of the lymphatic tree. Unfortunately, it was not possible to obtain samples of lymph from the smaller lymph channels. Therefore, the possibility remains that the metabolic activity of the smaller lymph channels, i.e., those peripheral to the femoral and cervical ducts, may change the gaseous tensions of the lymph from the tissues. On the other hand, the low P_{O_2} values of lymph cannot be attributed to a loss of O_2 through the walls of these small vessels by diffusion since such a process would require the existence of lower O_2 tensions in the tissues surrounding the ducts than those observed in the lymph.

A more reasonable prospect is that the metabolic activity of the lymph nodes through which the lymph passes may modify the original gas tensions of the interstitial fluid. Indeed, since practically all lymph passes through these nodes (*25*), and since the nodes, which contain actively reproductive and metabolizing tissues, are the last tissue encountered by lymph before it enters the lymphatic tree, the possibility exists that the gas tensions of lymph collected from the large channels reflect the gas tensions of the lymph nodes, rather than the gas tensions of interstitial fluid. An appreciable P_{O_2} gradient between interstitial fluid and lymph seems unlikely, however, since the administration of corticosteroids in doses sufficient to cause involution of the lymph nodes to only 20 per cent of their original weight (*26*) did not alter the O_2 tensions of lymph.

Lymph as a measure of tissue gas tensions

It is generally agreed that lymph originates as interstitial fluid (27, 28). Since neither interstitial fluid nor peripheral lymph is available for direct sampling, the present study has not entirely excluded the possibility that interstitial fluid may differ somewhat from the sampled lymph in gaseous composition. The evidence of the present study, however, favors the view that the sampled lymph provides a reliable approximation not only of the gas tensions within the last tissue it traverses, i.e., the lymph nodes, but also a measure of the gas tensions of the interstitial fluid from which it was formed. In turn, the gas tensions within the cells may be expected either to equal the gas tensions of the interstitial fluid, or else to be lower in P_{O_2} and higher in P_{CO_2}.

Of particular interest in the present study is the observation that lymph from several different channels has approximately the same low P_{O_2}, although the tissues drained by these channels would be expected to differ in their metabolic activities. The sites drained by each of these channels and the contribution of these regional channels to the total lymph flow are indicated schematically in Figure 4. The consistently low P_{O_2} of lymph from these different channels suggests that some cells of the muscle and subcutaneous tissue of the lower extremity and neck, of the bowel, and of the liver have lower O_2 tensions than the corresponding venous blood. It should be emphasized that the present study supplies no information concerning the gas tensions of the brain, the thoracic viscera, and other abdominal viscera, all of which contribute lymph in insufficient quantities to affect the composition of thoracic duct lymph.

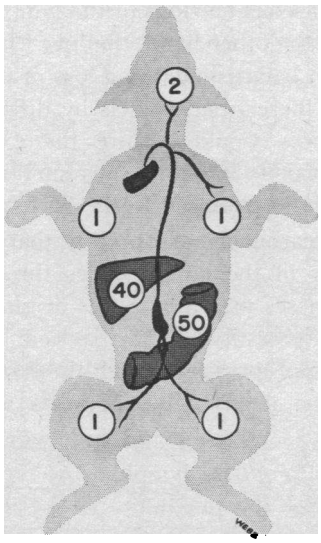

FIG. 4. THE SOURCES OF THORACIC DUCT LYMPH IN THE FASTING DOG (26). The number in each circle refers to the percentage of the total lymph flow contributed by the labeled organ or part. The gas tensions of lymph from the femoral duct represent the muscles and other tissues of the leg, the gas tensions of the cervical duct represent the tissues of the head excluding the brain, the gas tensions of lymph from the cysterna chyli represent the small bowel, and the gas tensions of the thoracic duct in the neck represent the difference between small bowel and liver.

If we assume that lymph in the large channels is relatively unaltered interstitial fluid, it is uncertain whether the gas tensions of lymph represent the mean gas tensions in the tissues of an organ or merely the gas tensions of the areas that are farthest from the blood capillary. In the case of the liver, the histological evidence of Sabin (29) makes it clear that hepatic lymph is derived largely from the periphery of the lobule, i.e., from areas remote from the major blood supply in the central vein. On the other hand, these same studies indicate that the lymphatic capillaries of muscle and subcutaneous tissues are randomly distributed with respect to blood capillaries, thereby affording equal opportunities for interstitial fluid from parts of the tissues both near to and far from the blood capillaries to be represented in the lymph sampled from the larger lymphatic channels.

Accordingly, mean tissue O_2 tensions of 8 mm Hg, based on values of lymph found in the present study, imply not only that cells adjacent to the blood capillaries have higher O_2 tensions, but also that the O_2 tensions of cells remote from the capillary may approach zero. The prospect that fluid bathing cells distant from the systemic capillary is low in O_2 tension was first considered by Krogh, who based his calculations on the capillary density of resting muscle (30) and reasonable values for the rates of diffusion and consumption of O_2 in muscle (31). That the O_2 tensions of parts of the tissues may actually reach zero is suggested by the association of high lactate values with the low values for O_2 tension in lymph, since it has been demonstrated that cells continue to op-

erate aerobically as long as the ambient O_2 tensions exceeds 1 mm Hg (32). Finally, the demonstration that the rate of perfusion of resting muscle varies continually from region to region because of intermittent capillary patency (33) suggests that oxygen poverty is only periodically confined to one portion of a tissue.

SUMMARY

1. The concentrations of the respiratory gases in interstitial fluid and tissues were estimated by measurements of the gaseous tensions of lymph collected from different lymphatic ducts. This approach assumes that lymph is interstitial fluid which has bathed tissues prior to its entry into the lymphatic tree and that it undergoes no modification in gas tensions between its site of origin and collection. When compared with other methods of measuring the gaseous tensions of tissues, it has the advantage of avoiding trauma to tissues and blood vessels and of providing a biological fluid in which CO_2 and O_2 tensions can be precisely measured.

2. The analysis of lymph from these different organs yielded CO_2 tensions which were uniformly higher than those of regional venous blood and O_2 tensions which were not only lower than those of venous blood, but averaged 8 mm Hg. It was demonstrated that these gas tensions of lymph could not be attributed to the metabolism of tissues of the larger lymphatic vessels or to an unsteady state of gas exchange.

3. The low O_2 tensions of the lymph, together with its high lactate values, indicate not only that the bulk of the tissues represented in the lymph (liver, small bowel, and skeletal muscle) operate at O_2 tensions far lower than those of venous blood, but also that in some parts of these tissues the tissue O_2 tension approximates 0 mm Hg.

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