JCI The Journal of Clinical Investigation

THE CHARACTERISTICS OF THORACIC DUCT LYMPH IN MAN

H. R. Bierman, … , Grace Singer, Fauno Cordes

J Clin Invest. 1953;32(7):637-649. https://doi.org/10.1172/JCI102776.

Research Article

THE CHARACTERISTICS OF THORACIC DUCT LYMPH IN MAN

By H. R. BIERMAN, R. L. BYRON, Jr., K. H. KELLY, R. S. GILFILLAN, L. P. WHITE, N. E. FREEMAN, and N. L. PETRAKIS, with the technical assistance of GRACE SINGER and FAUNO CORDES

(From the Laboratory of Experimental Oncology, National Cancer Institute, National Institutes of Health, Public Health Service, Federal Security Agency; the Department of Medicine and Cancer Research Institute, University of California School of Medicine; and the Department of Surgery, University of California School of Medicine, San Francisco, Cal.)

(Submitted for publication January 17, 1953; accepted April 4, 1953)

The thoracic duct is generally accepted as the major pathway of lymphocytes enroute to the circulating blood (1, 2, 3), accounting for approximately 70 per cent of all the lymphocytes in the peripheral blood. The remainder of the lymphocytes are said to enter the blood directly via the lymph from other sites (2). Reliable information concerning the hematologic content of lymph in the thoracic duct of man has been fragmentary and limited to chance observations in few patients (4).

The thoracic duct lymph is reported to flow from one to six hours after death (5, 6). Consequently, an attempt was made to study the cellular components of human lymph obtained by cannulation of the thoracic duct within one hour after death and then *in vivo* if a feasible technic could be developed (7). Volumetric measurements of the flow of lymph in addition would permit an estimation of the number of cells delivered per unit time into the peripheral circulation via the thoracic duct (8). Since at least two thoracic ducts are present in man in addition to innumerable other lymph-to-blood connections, it was realized that these anatomical considerations seriously limited the interpretation of single samples. Consequently cannulation of the major thoracic duct for continuous drainage over prolonged periods was undertaken.

PATIENTS AND METHODS

The thoracic ducts of 16 cadavers were isolated within one hour after death. Satisfactory flow of lymph fluid was obtained in 11 of these necropsy cases, 10 of whom had a form of leukemia. The hematologic findings were contrary to that expected from a review of the literature. Because of a valid criticism of any interpretation derived from *post mortem* material, the study was extended to living man (Figure 1).

Studies were performed on 10 patients, all of whom were far advanced in the course of their neoplastic disease, and all of whom volunteered as subjects after being informed of the proposed study. Four patients had leukemia, and six had other malignancies. Four ounces of milk and cream were given orally one-half hour prior to the procedure to aid in the identification of the duct. Polythene tubing, 2 to 3 mm. in external diameter, was introduced 3 to 5 cm. into the proximal segment of the thoracic duct pointing retrograde as it approached the left internal jugular-subclavian vein junction. The segment of the duct emptying into the venous junction was ligated. The polythene tubing pointing medially and inferiorly was securely tied in place after flow was established. The skin was closed with interrupted sutures without approximating the deeper layers. The tubing was fixed by sutures within the edges of the wound as it was closed.

The lymph was collected by gravity drip into sterile, silicone-lined glass containers. Heparin was employed exclusively as the anticoagulant. Samples for hematologic or chemical determinations were collected as separate fresh specimens. All counts and determinations were done as promptly as possible employing NBS certified hemocytometers and Trenner automatic filling pipets. In counts between 5,000 to 10,000 per cu. ml., counting all nine squares on each of two chambers from a single pipet, the 70 per cent confidence limits of the value obtained were $\pm$ 8.5 per cent. Peripheral venous blood was taken simultaneously for comparison. In the patients studied *post mortem,* blood for comparison had been obtained either just before death or by cardiac puncture after death.

In five instances, the thoracic duct was outlined *in vivo* by the retrograde introduction of Diodrast or Thorotrast (Figures 2A, B, C, D).

Whole blood or plasma was employed to replace the draining lymph, usually volume for volume. After the period of the lymph drainage was completed, the tubing was sealed and the lymph within was allowed to clot. The tube was uneventfully withdrawn 3 to 10 days later.

RESULTS

Studies post mortem. Attempts to locate the thoracic duct *post mortem* were uniformly unsuccessful unless half cream-half milk had been ingested 3 to 24 hours before cannulation. Satisfactory lymph flow was obtained in 11 patients, 10

of whom had leukemia (Table I). In eight patients, the blood leukocyte level exceeded the leukocyte level of the thoracic duct lymph; in two patients the reverse was found to be true. The leukocyte counts were the same in the lymph and blood of the remaining patient.

Studies in vivo. The thoracic duct was clearly distinguishable *in vivo* when the cream and milk were given 15 to 30 minutes before surgical exploration of the duct area. Thoracic duct lymph was obtained for continuous periods of 2 to 13 days in 10 patients (Table II, Figure 3). The polythene tube caused no untoward reaction during or after the period of drainage and did not seriously impair motion of the head or neck or cause discomfort after the first 24 or 48 hours. Delayed healing of the wound occurred in an area which had been repeatedly treated with intensive X-radiation in a single patient (KIN) who had advanced Hodgkin's disease. No evidence of a chylous fistula appeared in any case. One patient experienced transient syncope during the introduction of 70 per cent Diodrast into the thoracic duct although intravenous testing had shown no sensitivity.

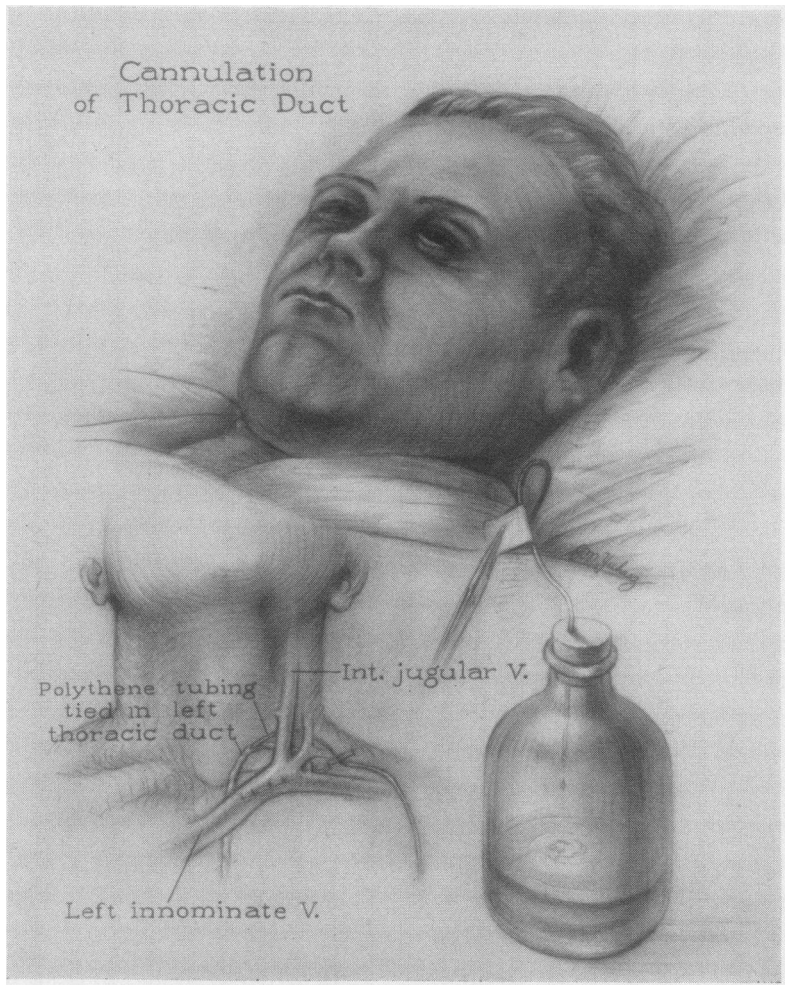

FIG. 1. CANNULATION OF THE THORACIC DUCT
The lymph is collected in sterile containers by gravity drip.

Appearance and flow characteristics. The lymph of the non-leukemic and leukemic patients had an opalescent appearance resembling skimmed milk, varying between a thick creamy and a thin watery consistency. Cream appeared within 10 to 20

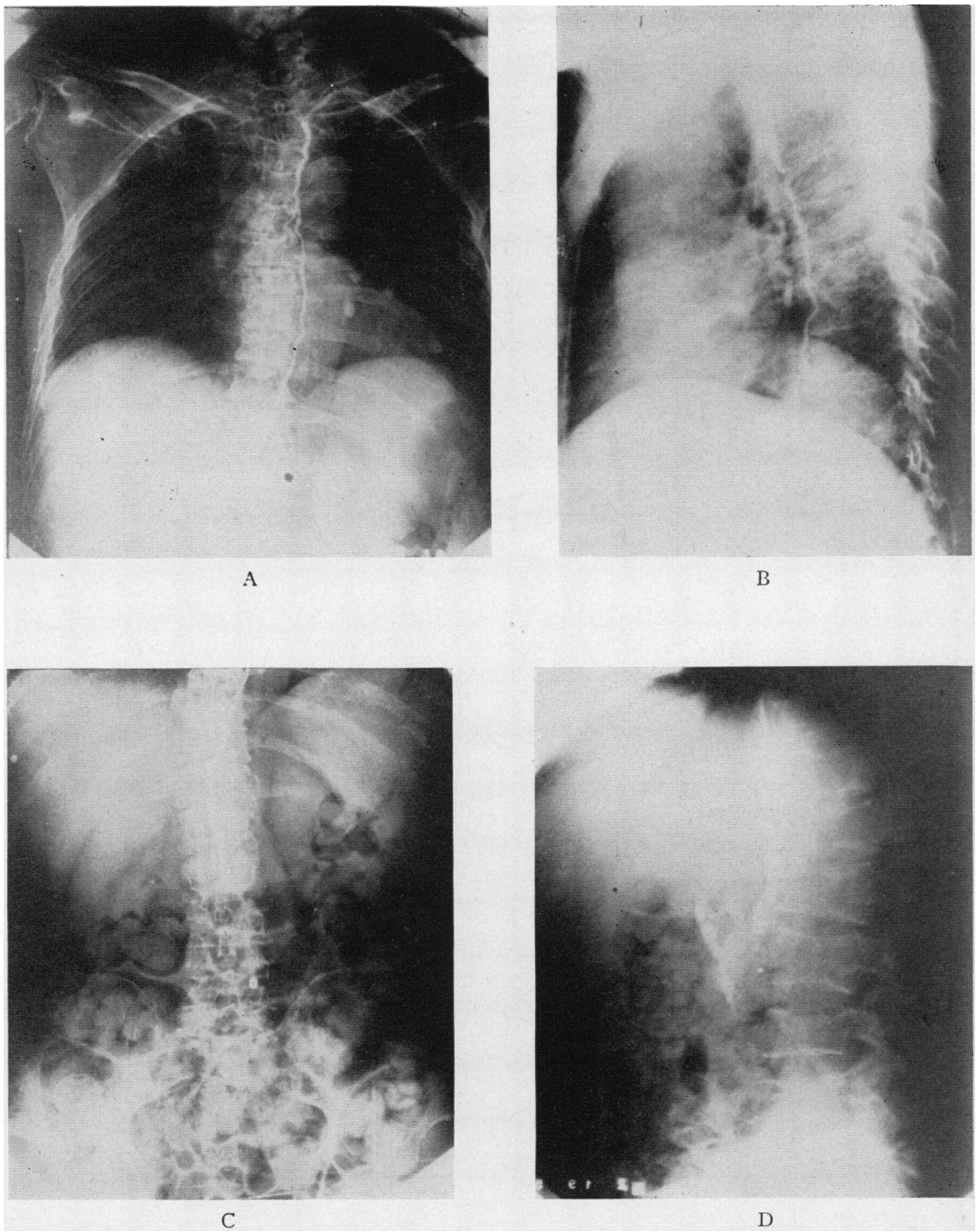

FIG. 2

A. Outline of thoracic duct in thorax following retrograde introduction of 75 per cent Diodrast.

B. Lateral view.

C. Anterior view of abdominal portion of the thoracic duct. The marker "O" is at the umbilicus.

D. Lateral view of abdominal portion. Note filling anteriorly of what is presumed to be mesenteric lymphatics.

TABLE I

Hematological data of thoracic duct lymph of eleven patients obtained at post mortem compared with venous blood

Name, Sex, Age	LIB F 3		LEF F 11		CUM M 11		DEM M 19		KAN F 35		JOH M 51		
Diagnosis	Lymphatic leukemia		Lymphatic leukemia		Lymphatic leukemia		Lymphatic leukemia		Lymphatic leukemia		Lymphatic leukemia		
	Lymph	Blood	Lymph	Blood	Lymph	Blood	Lymph	Blood	Lymph	Blood	Lymph	Blood	
Sample site	Thoracic duct	Finger, 1 hr.*	Thoracic duct	Finger, 1 hr.*	Thoracic duct	Cardiac	Thoracic duct	Cardiac	Thoracic duct	Cardiac	Thoracic duct	Vein, 5 hrs.*	Pericardial fluid
RBC	650,000		460,000	Hbg., 5.8 gms.	580,000	1,900,000	100,000	1,250,000	400,000	1,160,000	770,000	2,680,000	30,000
Platelets			80,000					130,000	30,000	40,000		60,000	
WBC	50,200	50,000	241,000	322,000	100	800	6,550	330,000	82,000	500,000	3,600	800	1,900
Differentials in per cent													
PMN		1				4 seen			6	5		76	
Meta										2			
Myl								2		3			
Lymphs, small	80	99	80	80	20 seen	16 seen	94	13	80	32	100	22	
large	20		20	20			6	85	58	58			
Others					1 normoblast	1 normoblast						2 monocytes	

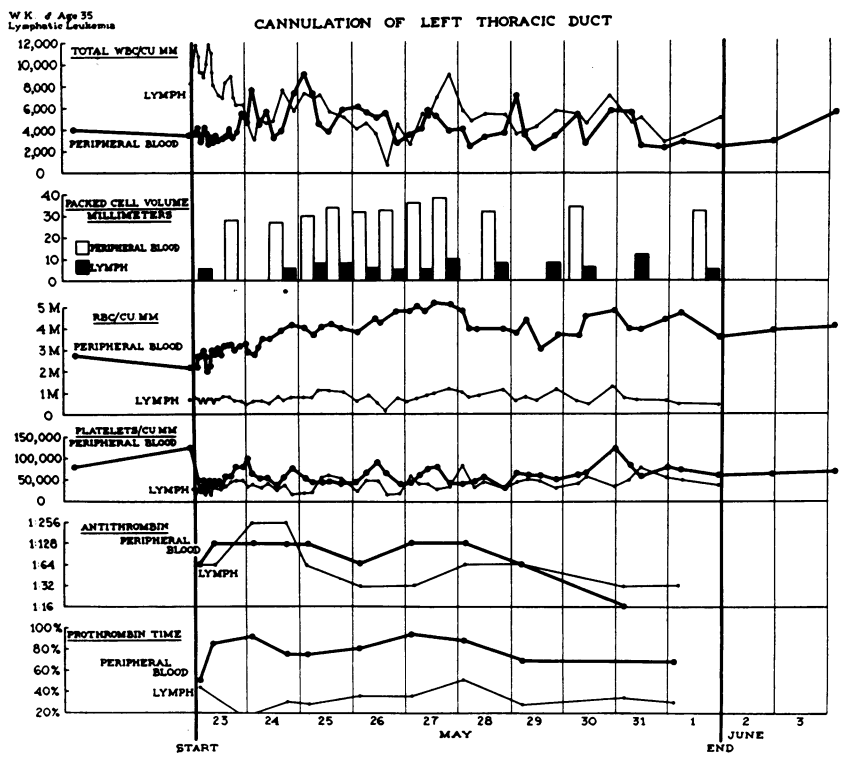

FIG. 3. HEMATOLOGICAL DATA DURING A REPRESENTATIVE STUDY ON KIR, 35-YEAR-OLD MAN WITH SUBLEUKEMIC LYMPHATIC LEUKEMIA

Note that the blood and lymph leukocyte counts approximate one another closely except for the first 24 hours.

TABLE I—*Continued*

Name, Sex, Age	PIT M 66		VAL F 68		SPI M 47		COO M 49		LIN M 58	
Diagnosis	Lymphatic leukemia		Lymphatic leukemia		Myelogenous leukemia		Myelogenous leukemia		Malignant melanoma	
	Lymph	Blood	Lymph	Blood	Lymph	Blood	Lymph	Blood	Lymph	Blood
Sample site	Thoracic duct	Ear, 5 hrs.*	Thoracic duct	Finger, 1 hr.*	Thoracic duct	Cardiac	Thoracic duct	Ear, 2 days*	Thoracic duct	Ear, 4 hrs.*
RBC	240,000	Hbg., 8.0 gms.	350,000	3,260,000	280,000	1,580,000	740,000	Hbg., 11.8 gms.	36,000	2,130,000
Platelets		80,000	10,000	55,000	10,000	10,000				100,000
WBC	55,000	289,000	35,600	381,000	3,000†	403,000	80,000	18,450	2,700	10,500
Differentials in per cent										
PMN			2		70	31	2	13	5‡	86
Meta				2				31		2
Myl			1	1		68	38	16		1
Lymphs, small	100	100	93	95	30	1	60	34	3	11
large			4	2					2	
Others								PMB, 3 PME, 3		

* Before death.
† One cc. sample obtained diluted by 0.2 cc. of heparin. Counts were not corrected for this dilution.
‡ Ten cells were differentiated. The remainder of the leukocytes showed degenerative changes. The erythrocytes appeared unaltered.

minutes after oral ingestion. In the leukemic patients, the lymph was more often blood-tinged, related to its content of erythrocytes (Table II).

The flow of lymph varied from 300 to 2,800 ml. of fluid per 24 hours (Figure 4). Free flow of lymph was obtained and measured accurately in six patients in whom the lymph content of leukocytes was also determined, thereby permitting an estimation of the number of cells passing through the thoracic duct ostensibly for delivery into the peripheral circulation (Table III). Cannulation of the right thoracic duct in patient ELM 36 hours

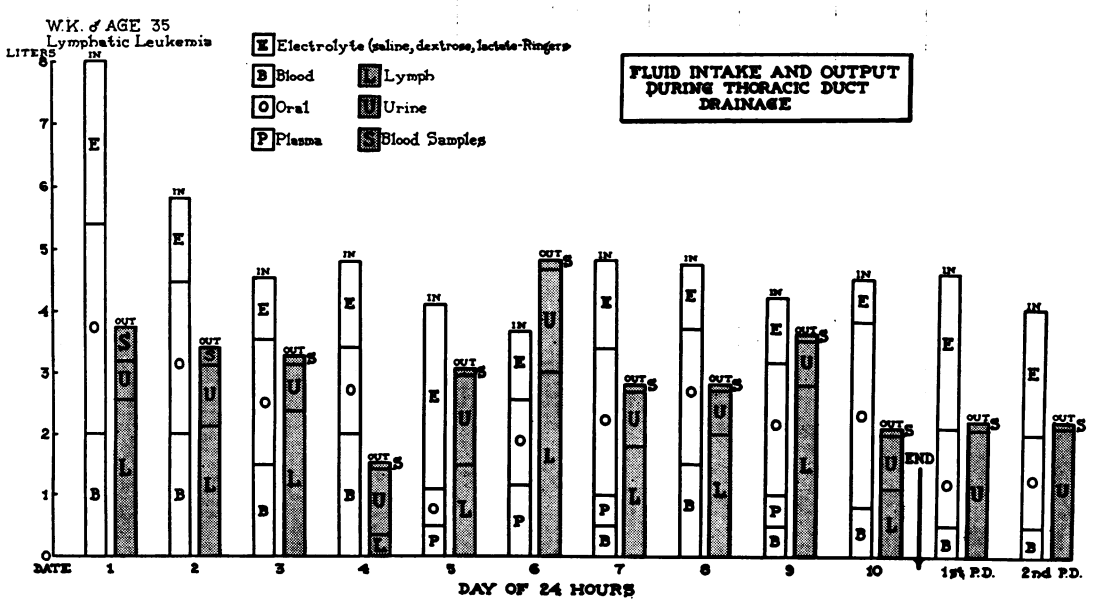

FIG. 4. DATA ON LYMPH FLOW AND FLUID REPLACEMENT DURING STUDY ON PATIENT KIR
The fear of significant fluid loss failed to materialize under this regimen of replacement.

TABLE II

Hematological data of thoracic duct lymph and venous blood on 10 patients obtained in vivo

Name, Sex, Age	ELM M 71		FLU F 75		KIR M 35		RAL M 16		HAL M 49	
Diagnosis	Lymphatic leukemia		Lymphatic leukemia		Subleukemic lymphatic leukemia		Myeloblastic leukemia with chloroma		Multiple myeloma	
Drainage period	2 days		3 days		11 days		4 days		13 days	
	Highest lymph count	Corresponding blood	Highest lymph count	Corresponding blood	Highest lymph count	Corresponding blood	Highest lymph count	Corresponding blood	Highest lymph count	Corresponding blood
RBC	156,000	2,690,000	99,000	4,070,000	790,000	2,280,000	450,000	2,390,000	35,000	3,950,000
Platelets	4,500	25,000	4,500	95,000	25,000	25,000	15,000	130,000	95,000	125,000
WBC	6,200	49,000	40,600	166,000	11,900	2,800	27,200	67,000	3,300	2,600
Differentials in per cent:										
PMN				11		11	1	12	1	67
Meta								2		
Myl								44		
PME				5	1	1				5
Lymphs:										
small	100	100	100	83	99	85	87	22	98	16
young							11	20		
Mono				1		3	1			11
Others									Plasma cell, 1	PMB, 1
	Lowest lymph count	Corresponding blood	Lowest lymph count	Corresponding blood	Lowest lymph count	Corresponding blood	Lowest lymph count	Corresponding blood	Lowest lymph count	Corresponding blood
RBC	174,000	2,380,000	6,300	3,000,000	150,000	4,390,000	100,000	2,080,000	5,000	4,030,000
Platelets	2,500	25,000	4,000	90,000	5,000	60,000	20,000	110,000	5,000	85,000
WBC	3,900	39,000	17,800	121,000	600	4,200	10,000	42,100	210	1,900
Differentials in per cent:										
PMN				2	1	16		10		64
Meta							1	2		
Myl		1						2		
PME								1		
Lymphs:										
small	100	99	100	98	99	84	93	38	4 seen	28
young							6	25		
Mono								2		8
Others										
	Corresponding lymph	Highest blood count	Corresponding lymph	Highest blood count	Corresponding lymph	Highest blood count	Corresponding lymph	Highest blood count	Corresponding lymph	Highest blood count
RBC	156,000	2,690,000	99,000	4,070,000	895,000	3,720,000	450,000	2,390,000	35,000	3,490,000
Platelets	4,500	25,000	4,500	95,000	25,000	45,000	15,000	130,000	10,000	95,000
WBC	6,200	49,000	40,600	166,000	6,900	8,500	27,200	67,000	1,200	8,300
Differentials in per cent:										
PMN				11	1	13	1	12		80
Meta								2		
Myl								44		
PME				5						3
Lymphs:										
small	100	100	100	83	99	87	87	22	100	5
young							11	20		
Mono				1			1			10
Others										PMB, 1 Plasma cell, 1
	Corresponding lymph	Lowest blood count	Corresponding lymph	Lowest blood count	Corresponding lymph	Lowest blood count	Corresponding lymph	Lowest blood count	Corresponding lymph	Lowest blood count
RBC	132,500	2,630,000	6,300	3,000,000	7,900,000	4,400,000	245,000	3,110,000	5,000	4,030,000
Platelets	2,000	25,000	4,000	90,000	55,000	75,000	45,000	75,000	5,000	85,000
WBC	4,000	25,000	17,000	121,000	2,500	2,100	22,700	23,800	210	1,900
Differentials in per cent:										
PMN				2	4	20		28		
Meta	1							3		
Myl								3		
PME						1				
Lymphs:										
small	99	100	100	98	96	79	98	21	4 seen	
young							2	44		
Mono								1		
Others										

after the left thoracic duct had been ligated did not significantly alter the circulating lymphocyte count.

Cellular characteristics. In general the leukocyte counts in lymph and venous blood in the living patient were the same as found in the *post mortem* studies. The peripheral blood leukocyte count in one patient with chronic lymphocytic leukemia (FLU) varied from 121,000 to 166,000 per cmm., and the comparable leukocyte counts in the lymph were 17,800 to 40,600 per cmm. In another pa-

TABLE II—*Continued*

Name, Sex, Age	CLI F 56		KIN M 16		BUT M 54		BEA M 62		DAV F 28	
Diagnosis	Multiple myeloma		Hodgkin's disease		Carcinoma mouth		Carcinoma neck		Lymphosarcoma	
Drainage period	24 hours		5 days		7 days		3 days		10 days	
	Highest lymph count	Corresponding blood	Highest lymph count	Corresponding blood	Highest lymph count	Corresponding blood	Highest lymph count	Corresponding blood	Highest lymph count	Corresponding blood
RBC	1,000	2,670,000	70,000	3,580,000	7,500	4,330,000	2,000	3,740,000	5,000	6,400,000
Platelets	5,000	60,000	50,000	170,000	10,500	295,000	2,000	215,000		
WBC	2,900	1,800	400	6,500	3,500	5,600	5,600	7,900	900	7,600
Differentials in per cent:										
PMN		59	9 seen	94		95		88		86
Meta										
Myl										
PME						1		2		5
Lymphs:										
small	100	30	1 seen	6	100	2	100	10	100	9
young										
Mono		11				2				
Others										
	Lowest lymph count	Corresponding blood	Lowest lymph count	Corresponding blood	Lowest lymph count	Corresponding blood	Lowest lymph count	Corresponding blood	Lowest lymph count	Corresponding blood
RBC	700	2,220,000	24,500	3,080,000			5,000	3,980,000	few	4,480,000
Platelets	2,000	90,000	8,000	130,000			5,500	210,000		
WBC	1,100	2,400	11	3,600	1,600	4,800	4,000	7,900	None seen	7,000
Differentials in per cent:										
PMN		46		87		83		76		83
Meta										
Myl										
PME				1		1				7.5
Lymphs:										
small	100	50	1 seen	2	100	9	100	20		5
young										
Mono		2		10		7		4		3.5
Others		Plasma cells, 2								PMB, 1
	Corresponding lymph	Highest blood count	Corresponding lymph	Highest blood count	Corresponding lymph	Highest blood count	Corresponding lymph	Highest blood count	Corresponding lymph	Highest blood count
RBC	700	2,220,000	70,000	3,580,000	8,000	4,760,000	5,000	3,980,000	5,000	6,400,000
Platelets	200	90,000	50,000	170,000	1,000	200,000	5,500	210,000		
WBC	1,100	2,400	400	6,500	3,000	10,300	4,000	7,900	900	7,600
Differentials in per cent:										
PMN		46	9 seen	94		94		76		86
Meta										
Myl										
PME										
Lymphs:										
small	100	50	1 seen	6	100	2	100	20	100	9
young										
Mono		2				4		4		
Others		Plasma cells, 2								
	Corresponding lymph	Lowest blood count	Corresponding lymph	Lowest blood count	Corresponding lymph	Lowest blood count	Corresponding lymph	Lowest blood count	Corresponding lymph	Lowest blood count
RBC	1,000	2,670,000	11,500	3,790,000			6,000	3,240,000	few	4,480,000
Platelets	5,000	60,000	4,000	170,000			1,500	205,000		
WBC	2,900	1,800	150	3,200	1,600	4,800	4,500	5,800	None seen	7,000
Differentials in per cent:										
PMN		59	1 seen	69		83		84		83
Meta										
Myl										
PME				1		1		1		7.5
Lymphs:										
small	100	30	1 seen	6	100	9	100	12		5
young			1 seen							
Mono		11		24		7		3		3.5
Others										PMB, 1

tient who had the same disease (ELM) the peripheral blood leukocyte number fluctuated between 25,000 and 49,000 per cmm., while that in the lymph was found to be 4,200 to 6,200 per cmm. The differential leukocyte counts showed smaller total numbers of lymphocytes in the lymph than in the blood in both cases (Table II).

On two occasions, the leukocyte level of the lymph initially exceeded that found in the venous blood. In one patient (KIR) with subleukemic lymphocytic leukemia, except for the first 24 hours, the leukocyte contents of the lymph and blood both varied considerably but in general were approximately the same (Figure 3). Similarly, in another

TABLE III

Calculated total leukocyte flow from the thoracic duct in six patients compared to leukocyte number in the peripheral blood

Patient	Diagnosis	Period of flow	Flow per 24 hours ml.	Average leukocyte count per cmm.		Total leukocyte flow per 24 hours in the lymph	Body weight in Kg.	Total leukocyte number in peripheral blood†
				In lymph	In blood			
FLU	Lymphatic leukemia	2 days	1,100	25,500	135,000	28.1×10^9	59.5	56.2×10^{10}
ELM	Lymphatic leukemia*	6 hours	900	4,800	38,000	4.3×10^9	49.9	13.3×10^{10}
KIR	Lymphatic leukemia	10 days	2,000	5,400	6,000	10.8×10^9	68.0	28.5×10^9
RAL	Myeloblastic leukemia	2 days	1,000	19,500	33,500	19.5×10^9	78.5	18.4×10^{10}
KIN	Hodgkin's disease	3 days	475	200	5,500	9.5×10^7	48.5	18.7×10^9
HAL	Multiple myeloma	12 days	800	2,100	3,500	1.7×10^9	59.0	14.5×10^9

* Right thoracic duct—major lymphatics in the vicinity of the left jugular-subclavian junction had been ligated 48 hours previously.

† Calculated from blood volume estimated at 7 per cent of body weight.

patient (RAL), a 16-year-old boy with a fulminant myeloblastic leukemia associated with chloromatous tumor formation, the cells in the lymph were predominantly small mature lymphocytes which had no consistent numerical relationship to either the total number or differential leukocyte count in the peripheral blood.

The leukocyte content of the thoracic duct lymph in the non-leukemic patients in this study varied from 210 to 5,600 per cmm. In three patients with leukemia the lymph leukocyte count was within the normal limits. In one patient (FLU) it was slightly higher than the upper limits of that reported for normal man (3). The lymph count in these four leukemic patients was approximately 10 to 100 per cent of that in the peripheral blood.

Chemical characteristics. Biochemical studies of simultaneously obtained lymph and venous blood *in vivo* were done on six patients. In four patients, daily or twice-daily samples were studied for 2 to 11 consecutive days (Table IV). The chemical constituents of the lymph and blood remained remarkably constant from day to day during the period of drainage. The globulin content of blood consistently exceeded that of the lymph in all patients and while the albumin content of the blood often exceeded that in the lymph the difference was neither as great nor as constant as that of the globulin (Table V). The total cholesterol content of blood was markedly higher than that in lymph, due primarily to the esterified fraction. The alkaline phosphatase and thymol turbidity determinations of the lymph were found to be 7 and 12 times higher respectively than that of the blood in one patient; in another patient the alkaline phosphatase values for blood and lymph were equal (Table V). The glucose content of lymph in one instance was significantly higher than that of blood.

There was no alteration in the clinical or hematological status, either exacerbation or improvement, in any patient following the procedure.

DISCUSSION

The leukocyte count in the thoracic duct in normal man varies from 2,000 to 20,000 per cmm. (3), consisting almost totally of lymphocytes (Figure 5). This is about 2 to 10 times the number of lymphocytes that can be found per cubic millimeter at any one time in the peripheral blood. The thoracic duct lymph in the normal subject is reported to flow between 1,500 and 2,200 cc. in each 24 hours which calculates to a delivery of approximately 35×10^9 cells per 24 hours into the peripheral circulation (3, 9). Since only one-third of this number can be accounted for in the peripheral blood, it has been assumed that the lymphocyte is replaced three times daily and that the intravascular life span of the lymphocyte can be calculated therefrom (8, 10, 11). Calculations of life span of lymphocytes in the peripheral circulation by this method are based upon the premise of a single securely closed circulation consisting of the flow of lymphocytes from the production site through the thoracic duct into the blood and thence to destruction. There is no consideration of rapid removal by sequestration (12), recirculation in some organ (13), or return of lymphocytes from the peripheral blood back into the lymphatic system (14). If such calculations are valid (and there are many reasons to doubt it) (10), the life span of the lymphocytes in most of these leukemic patients would be expected to be longer than in the

TABLE IV

Biochemical data of blood and lymph during thoracic duct cannulation in patient KIR, m., age 35—lymphatic leukemia

Blood

	5-22	5-23			5-24			5-25		5-26		5-27		5-28		5-29	5-30	5-31	6-2	6-3	6-4	6-5	6-6	6-8	6-12	
	9:00 a.m.	11:30 a.m.	3:00 p.m.	11:00 p.m.	12:30 a.m.	8:45 a.m.	9:00 p.m.	8:00 a.m.	3:30 p.m.	8:40 a.m.	3:15 p.m.	9:00 a.m.	3:45 p.m.	8:30 a.m.	1:30 p.m.	9:00 a.m.	1:30 p.m.	8:30 a.m.	8:30 a.m.	9:00 a.m.	9:00 a.m.	9:00 a.m.	9:00 a.m.	9:00 a.m.	9:00 a.m.	3:00 p.m.
Chlorides	109.9	107.1	107.	112.4		107.	106.2	108.	108.	102.8	105.	104.5	103.6	103.5	103.5	103.5	107.1	104.	103.	106.2	98.2	102.		103.	100.	106.2
NPN	34.8	38.9	33.8	36.8		36.8	35.2	33.8	37.4	32.5	34.0	25.0	23.7	24.3	24.68	27.73	33.4	36.4	31.1	20.4	21.7	30.4	27.8	28.2	23.9	25.7
Total protein	6.31	5.72	6.02	5.57		5.01	4.52	5.16	5.23	5.52	4.94	5.20	4.93	5.2	5.10	5.73	5.40	5.27	5.06	5.82	5.70	5.96	6.17	5.61	5.53	5.13
Albumin	4.07	3.79	3.69	3.38		3.22	2.79	2.95	3.00	2.92	3.02	3.09	2.96	2.7	2.79	3.28	2.92	3.12	2.76	3.10	3.38	3.89	3.42	3.49	3.40	3.13
Globulin	2.24	1.93	2.33	2.19		1.79	1.73	2.21	2.23	2.60	1.92	2.11	1.97	2.5	2.31	2.45	2.48	2.15	2.30	2.72	2.32	2.07	2.75	2.12	2.13	2.00
Sodium	136.7	134.0	129.	133.		130.	130.	130.	133.	138.	142.	36.		132.3		136.5		141.	134.1	131.	137.	135.	135.	131.	131.2	131.2
Potassium	4.7	4.4	4.5	4.9		4.7	4.4	4.9	4.5	4.3	4.9	4.3		4.3		4.9		4.4	5.07	4.7	4.3	4.6	4.5	4.8	3.7	4.5
Uric acid	4.5	4.06	4.10	3.7		3.40	3.46	3.34	3.34	3.20	3.50	3.34	3.50	3.80	3.54	3.34	3.84	4.00	4.16	3.28	3.08	3.92	QNS	4.66	4.04	3.24
Calcium	9.81	8.84	10.42	10.39		8.63	8.74	8.63	9.34	8.63	8.26	QNS	10.70	9.17	8.67	QNS	9.86	8.99	9.33	9.11	9.36	9.91	9.98	9.43	9.47	9.34
Phosphorus	3.25	3.58	4.3	4.4		3.77	3.40	QNS	4.75	3.20	3.82	2.42	QNS	3.92	3.22	3.10	4.77	3.20	3.07	3.15	3.05	QNS	QNS	3.83	3.72	3.96
Glucose			77.0	93.5		82.5		82.8	75.1	71.3	D.C.															
Creatinine	1.11	1.20	1.04			1.13				0.95		0.97		1.10		0.97										
Total	121.		92.5	115.4		100.4	100.4		98.7	103.			106.	92.2		QNS	92.2	97.8	121.4	97.8	123.	121.	QNS	98.51	04.0	75.6
Cholesterol free	28.6	QNS	31.8	27.9		29.7	29.7		25.1	31.9		QNS	37.6	26.7			33.6	28.7	35.6	47.7	46.1	42.2	104.0	42.6	40.6	31.8

Lymph

Chlorides		105.	108.	100.9	104.4	109.	104.4	108.	99.1	105.3		113.3	105.3	105.3	107.1	101.8	98.3	108.	105.	
NPN		39.9	38.7	28.4	39.3	38.1	35.9	36.4	37.44	34.24		26.8	23.7	26.5	24.91	27.86	32.0	33.7	33.0	
Total protein		4.25	3.95	3.76	3.94	2.92	2.72	2.82	3.33	3.00		2.82	2.58	3.21	2.21	3.35	2.85	2.83	3.04	
Albumin			2.62	2.53	2.65	2.02	1.75	1.78	1.98	1.92		1.93	1.79	2.26	1.47	2.14	1.75	1.87	1.97	
Globulin			1.33	1.23	1.29	0.90	0.97	1.04	1.35	1.08		0.89	0.79	0.95	0.74	1.21	1.10	0.96	1.07	
Sodium		142.	137.	133.	135.	136.	135.	136.	133.	136.		141.6		136.3		137.		141.6	123.2	
Potassium		4.7	4.5	4.9	4.8	4.9	4.4	4.7	4.5	4.6		4.8		4.9		5.3		4.1	4.7	
Uric acid			3.90	3.9	3.6	3.46	3.00	2.86	4.30	3.40		3.40	3.16	4.30	3.66	3.30	3.63	3.90	4.24	
Calcium		9.97	8.36	7.92	8.58	7.82	6.96	7.84	8.14	8.26		7.81	7.47	8.28	7.16	8.04	7.95	7.91	8.27	
Phosphorus			3.6	4.1	4.4	3.63	3.41	4.00	4.63	3.42		2.57	3.23	4.25	3.35	3.50	4.79	3.37	3.17	
Glucose			75.6	36.4	95.7	72.0		72.2	77.7	79.0										
Creatinine			1.04			0.97		0.99		1.03		1.02		1.13		1.06				
Total			62.0			63.7	58.4	47.4		50.5			42.2	38.3		52.4	68.0	56.3	66.5	
Cholesterol free			30.2			26.5	21.6	15.9		18.4			23.9	16.4		21.9	41.1	20.7	24.6	

TABLE V

Biochemical data on average blood and lymph obtained simultaneously

		Sodium	Potassium	Chloride	NPN	Uric acid	Creatinine	Total protein	Albumin	Globulin	Cholesterol mg.%		Phosphorus	Calcium	Glucose	Alk. phosphate	Thymol turbidity	Bilirubin	
		mEq./l.	mEq./l.	mEq./l.	mg.%	mg.%	mg.%	gm.%	gm.%	gm.%	Total	Free	mg.%	mg.%	mg.%			Total	Prompt
HAL	Blood	132	5.9	95	141	10.9	9.0	9.4	2.48	6.92	101.4	27.9	6.3	11.8	117				
	Lymph	132	5.6	96	139	10.8	8.9	7.33	2.53	4.80	64.6	26.8	6.4	11.1	136				
RAL	Blood	130	4.6	98	30	3.6	1.4	6.63	3.50	3.13	92.6	30.5	4.4	10.0					
	Lymph	131	4.4	103	26	3.3	1.3	4.25	2.61	1.64	55.6	26.0	3.9	7.8					
BEA	Blood	113	5.0	94	32	4.3	0.8	6.73	3.30	3.43	167	56	3.9	9.8					
	Lymph	118	4.8	87	30	4.1	0.8	4.60	2.40	2.20	98	51	3.6	8.2					
BUT	Blood	135	5.2	98	25.1	5.2	1.0	7.25	3.04	4.21	139	45	4.1	9.8		1.7	5.9	0.6	0.1
	Lymph	132	4.9	99	24.2	5.0	1.0	5.34	2.67	2.67	106	50	3.9	8.2		21.0	42.0	0.9	0.3
KIN	Blood	124	4.1	94	15.8	1.6		5.38	2.0	3.1	83	33	3.7	8.5		7.3		1.1	0.5
	Lymph	124	3.9	95	13.4	1.7		2.91	1.5	1.5	34	15	4.2	6.8		6.3		1.1	0.5

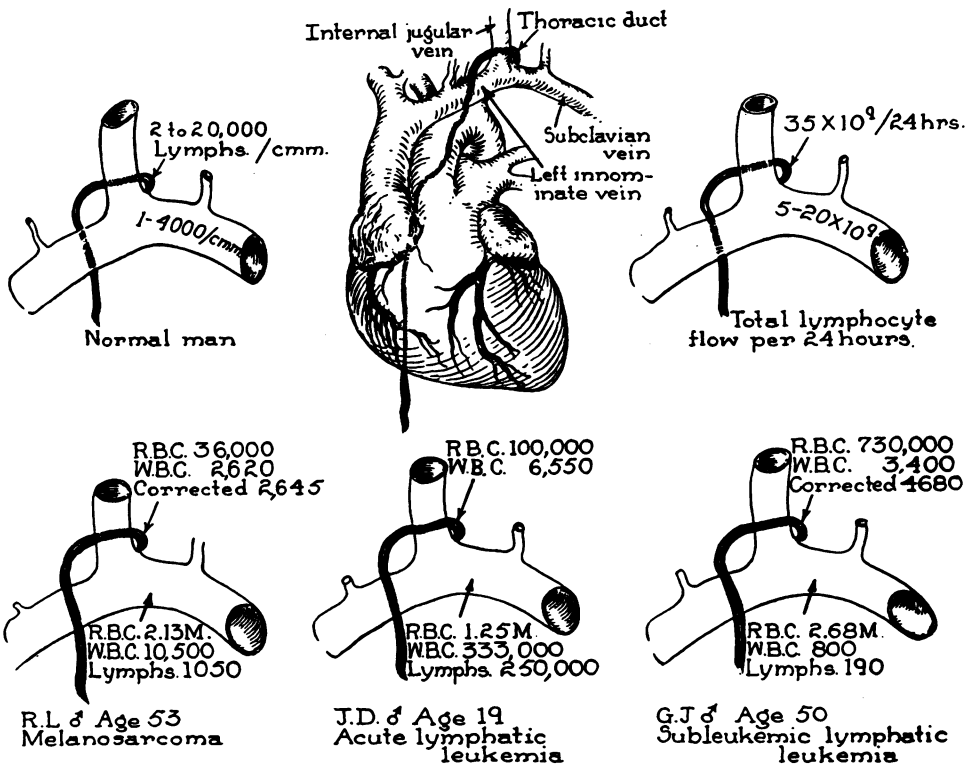

FIG. 5. SCHEMATIC REPRESENTATION OF NORMAL LYMPHOCYTE FLOW AS COMPARED WITH THAT FOUND IN A NON-LEUKEMIC PATIENT, AND TWO PATIENTS WITH LYMPHATIC LEUKEMIA, ONE WITH A HIGH PERIPHERAL BLOOD LEUKOCYTE COUNT AND ONE WITH A LEUKOPENIA

The normal flow of lymph through the thoracic duct in man is estimated at approximately 35 billion lymphocytes per 24 hours. The duct lymphocyte counts in the three patients are approximately the same despite marked differences in the peripheral blood. The corrected counts are those caused by possible dilution with peripheral blood and show little change.

non-leukemic individual (15, 16). This would suggest some defect in the normal destruction or removal of the lymphocyte in the leukemic patient which would be reflected in a longer than normal life span in the intravascular circulation. This prolongation of life of the circulating lymphocyte may reside within the properties of the cell (17), the host or both.

In dogs, rabbits and cats the ligation of both right and left thoracic ducts results in a prompt fall in the peripheral blood lymphocyte number (18, 19). Similar results have been obtained by diverting the lymph flow by thoracic duct cannulation (20, 21, 22). There was no significant fall in circulating lymphocyte number in the two day period of drainage in patient ELM in whom the right thoracic duct was cannulated after the major lymphatics in the left neck had been previously ligated. This would suggest that the life span of the lymphocytes in this patient with lymphatic leukemia was longer than the two days of drainage period or that his major portal of entry of lymphocytes was from a site other than the thoracic duct.

Approximately 5 per cent of all the cells in the lymph in these studies were found to be lymphoblasts which are rarely seen in the circulating blood in the normal individual. This absence of lymphoblasts suggests either a most rapid change within the blood to a small lymphocyte or prompt removal from the peripheral circulation. Similarly, there is a larger percentage of intermediate-sized lymphocytes in the lymph than are found circulating in normal man. It should be noted that the thoracic duct empties just proximal to the pulmonary circulation. Attempts to detect any increases in lymphocyte number by venous catheter sampling at or proximal to the thoracic duct opening met uniformly with failure (12). In the

patients with granulocytic and lymphocytic leukemia, granulocytes were found in considerable numbers in the lymph.

Significant numbers of erythrocytes in the lymph were present only in patients with the leukemias and, in general, reflected the hemorrhagic status of the patient. In those leukemic patients in whom transfusions were given to support a falling blood hemoglobin level, the erythrocyte count in the lymph also rose, particularly if there was little or no improvement of the hemorrhagic component. The factor of an increased permeability of the lymphatics or incompetent vein-duct valves in the leukemic patient also must be strongly entertained.

The data indicate that the number of leukocytes in the thoracic duct lymph in the patients studied usually was materially less than that of venous blood. Of particular significance was this finding in patients with lymphocytic leukemia with either high or low leukocyte counts in the peripheral blood. Similar findings occurred in one patient with myeloblastic leukemia. The non-leukemic patients in this study had fewer leukocytes in the lymph than reported for normal individuals (3, 4). The daily total volume of lymph flowing in the leukemic patients did not exceed that reported in normal subjects (3). Consequently, the total number of leukocytes entering the peripheral blood daily via the thoracic duct in the four leukemic cases in whom accurate lymph flow values were obtained did not exceed 35 billion leukocytes, the value reported by Drinker and Yoffey (3), to be entering the circulation in the normal subject.

The average number of leukocytes in the lymph of eight patients with lymphocytic leukemia, taking the highest count, was 64,600 per cmm. while the peripheral blood at the same time averaged 260,900. The ratio of the counts, lymph to blood, was 1 to 4. Six of these eight patients had lymph leukocyte counts exceeding the 2 to 20,000 per cmm. value reported by Drinker and Yoffey (3). Similarly, in seven non-leukemic patients the highest lymph count averaged 2,760 with the corresponding blood count averaging 6,070—a ratio of 1 to 2.3.

In his original description of leukemia (23), Virchow concluded that leukemia was a disease of overproduction of the leukocytes and shortly thereafter expanded this impression to include the thoracic duct as the route by which the excess number of cells entered the circulation (24). Since this time, many other investigators have accumulated other information which supports the concept of overproduction of leukocytes. These findings are not in accord with this concept of leukemia and create a valid doubt that the thoracic duct is the major pathway of delivery of the excessive numbers of leukocytes into the peripheral blood in all leukemias, or that the leukocytosis in the leukemic patients studied is always a result of an increased production of leukocytes delivered by the thoracic duct route. The possibility of other portals of entry for these cells have not been excluded in these studies. Also, the good possibility remains that there may be a constant variation between rates of production, delivery and removal which may make it fortuitous consistently to fail to obtain evidence of delivery of excessive numbers of cells via any route.

It should be emphasized that these data were obtained on relatively few patients and therefore may not thoroughly represent the variation in lymphocyte flow in man (9). While the numbers of leukocytes obtained in the thoracic duct lymph probably represent the minimum, since in all but one case only the left thoracic duct was cannulated, the avoidance of general anesthesia and the magnitude of the discrepancies between the findings in the lymph and venous blood support these interpretations. The further multiplication of cells by rapid division in the circulation after they leave the thoracic duct requires consideration before any further conclusions can be drawn.

SUMMARY

1. Thoracic duct lymph was collected from 11 cadavers within one hour after death, and from 10 patients during life for continuous periods of 2 to 13 days.

2. The leukocyte count of the lymph varied from 210 to 5,600 leukocytes per cmm. in six non-leukemic patients studied during life.

The lymphocyte count in lymph in the leukemic patients during life usually did not exceed the lymphocyte count in the venous blood. In one patient with subleukemic lymphocytic leukemia for the first of 11 days the leukocyte count of the lymph exceeded that of the peripheral blood.

3. The findings of the studies conducted *post mortem* in 11 patients, 10 of whom had leukemia, were similar to those obtained *in vivo*. In three patients, the lymph leukocyte count exceeded or equalled that in the blood. In the remaining eight patients, six of whom had lymphocytic leukemia, the peripheral blood leukocyte number exceeded that found in the lymph.

4. The erythrocyte number in the thoracic duct lymph obtained from patients with the leukemias was considerable, ranging up to 1.5 million per cmm. The erythrocyte count in the lymph of the non-leukemic patients was generally insignificant. The lymph platelet number varied considerably in both groups (1,000 to 95,000 per cmm.) and never rose to the level found in the venous blood.

5. The chemical composition of thoracic duct lymph closely approximated that of blood plasma with slightly reduced values for albumin and globulin. The antithrombin and prothrombin content of thoracic duct lymph in two patients in whom it was measured was comparable to that found in the venous blood. The cholesterol ester content of the lymph exceeded that of blood.

6. No beneficial or deleterious effects of the procedure were observed on the clinical or hematological course of the patients studied.

ACKNOWLEDGMENTS

The authors wish to acknowledge the assistance of Dr. W. O. Reinhardt, Miss Marjorie Brown, Mrs. Oma Mitchell and Mrs. Anna Lance.

REFERENCES

1. Drinker, C. K., and Field, M. E., Lymphatics, Lymph and Tissue Fluid. Williams & Wilkins, Baltimore, 1933.
2. Blalock, A., Robinson, C. S., Cunningham, R. S., and Gray, M. E., Experimental studies on lymphatic blockage. Arch. Surg., 1937, **34**, 1049.
3. Drinker, C. K., and Yoffey, J. M., Lymphatics, Lymph and Lymphoid Tissue. Harvard University Press, Cambridge, Mass., 1941.
4. Haedicke, J., Ueber polynukleäre neutrophile Lymphzellen (Ein Beitrag zur Lösung der Frage nach der Abstammung der Farblosen Blutzellen). Folia haematol., 1906, **3**, 527.
5. Bainbridge, F. A., The post-mortem flow of lymph. J. Physiol., 1906, **34**, 275.
6. Rouviere, H., and Valette, G., Physiologie du systeme lymphatique. "Formation de la lymphe, circulation lymphatique normale et pathologique." Masson et Cie, Paris, 1937. Cited in (4).
7. Bierman, H. R., Gilfillan, R. S., Kelly, K. H., Byron, R. L., Jr., and Freeman, N., Cannulation of the thoracic duct in man. Proc. Amer. Fed. Clin. Res., May 1951.
8. Yoffey, J. M., The quantitative study of lymphocyte production. J. Anat., 1932–1933, **67**, 250.
9. Yoffey, J. M., Variation in lymphocyte production. J. Anat., 1935–1936, **70**, 507.
10. Ehrich, W. E., The role of the lymphocyte in the circulation of the lymph. Ann. New York Acad. Sc., 1945–1946, **46**, 823.
11. Adams, W. S., Saunders, R. H., and Lawrence, J. S., Output of lymphocytes in cats including studies on thoracic duct lymph and peripheral blood. Am. J. Physiol., 1945, **144**, 297.
12. Lanman, J. T., Bierman, H. R., and Byron, R. L., Jr., Transfusion of leukemic leukocytes in man: hematologic and physiologic changes. Blood, 1950, **5**, 1099.
13. Bierman, H. R., Some principles underlying the pathological physiology of the leukemias in man. Proc. Second National Cancer Conference (sponsored jointly by the American Cancer Society and the National Cancer Institute, Cincinnati, March 1952), in press.
14. Clark, E. R., and Clark, E. L., Observations on living mammalian lymphatic capillaries—their relation to the blood vessels. Am. J. Anat., 1936–1937, **60**, 253.
15. Kline, D. L., and Cliffton, E. E., The life span of leucocytes in the human. Science, 1952, **115**, 9.
16. Osgood, E. E., Tivey, H., Davison, K. B., Seaman, A. J., and Li, J. G., The relative rates of formation of new leukocytes in patients with acute and chronic leukemias measured by the uptake of radioactive phosphorus in the isolated desoxyribosenucleic acid. Cancer, 1952, **5**, 331.
17. Morrow, P. L., Bierman, H. R., and Jenkins, R., Effect of ultrasonic vibration on the formed elements of blood from normal and leukemic subjects. J. Nat. Cancer Inst., 1950, **10**, 843.
18. Bunting, C. H., and Huston, J., Fate of the lymphocyte. J. Exper. Med., 1921, **33**, 593.
19. Lee, F. C., Changes in the number of small lymphocytes of the blood following ligation of the thoracic duct. J. Exper. Med., 1922, **36**, 247.
20. Biedl, A., and von Decastello, A., Ueber Aenderungen des Blutbildes nach Unterbrechung des Lymphzuflusses. Arch. f. d. ges. Physiol., 1901, **86**, 259.
21. Banti, G., Sull'ufficio degli organi linfopoietico ed emopoietici nella genesi dei globuli bianchi del sangue. Cited in (14). Arch. fisiol., 1903–4, **i**, 241.
22. Kindwall, J. A., A supra-vital study of the cells in the lymph stream of the rabbit. Bull. Johns Hopkins Hosp., 1927, **40**, 39.
23. Virchow, R. L., (Weisses Blut). Neue Notizen a.d. Geb. d. Nat. Heilk. Weimar, 1845, **36**, 151.
24. Virchow, R., Cellular pathology as based upon physiological and pathological histology. De Witt Publisher, New York, 1858, pp. 204–205.