ficiency. 2) Cardiac contractile responses were also measured as increases in the force of left ventricular contraction above the initial level. Technical difficulties with the method precluded accurate comparison of initial contractile force, under conditions of identical fiber length and tension, between the control and experimental groups. 3) All measurements were made during anesthesia, with chest open, and during artificial respiration.

With the above limitations in mind, we conclude the following: 1) the adrenalectomized animals were in mild symptomatic adrenal insufficiency as indicated by general appearance and behavior, hypotension, and decreased tolerance to pentobarbital (the dose required for anesthesia being approximately one-half that required by controls). 2) Systemic and pulmonary hypotension is an early feature of experimental adrenal insufficiency. 3) There is no significant demonstrable impairment in pressor or cardiac contractile responses to norepinephrine in dogs with early (2 days) adrenal insufficiency which are not on replacement therapy. 4) The unimpaired cardiac contractile responses plus unimpaired pressor responses suggest, but do not prove, that the vascular responses to nor-epinephrine are also unimpaired. 5) The results afford no explanation for the hypotension present in adrenal insufficiency. Anatomical lesions in the heart do not necessarily accompany the hypotension.

Summary. Cardiovascular responses to norepinephrine have been studied in adrenalectomized and control dogs. The initial mean systolic and diastolic blood pressures of the adrenalectomized group in both femoral and pulmonary arteries were lower than those of the control group. There was no significant difference between the 2 groups in ability to respond to intravenously injected norepinephrine by an increase in force of cardiac contraction or by an increase in systemic or pulmonary blood pressure. Myocardial or coronary artery lesions did not occur in the 2 adrenalectomized animals examined.

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Retrograde and Forward Perfusion of Isolated Canine Lung Lobes.* (23913)

DUDLEY B. HOULE, GILBERT S. CAMPBELL AND MAURICE B. VISSCHER
Departments of Surgery and Physiology, University of Minnesota Medical School, Minneapolis

The influence of mechanical factors on pulmonary vascular resistance has become established during recent years. Since the pulmonary vascular bed is an easily distensible system, it is not surprising that changes in transmural pressure exert a major influence on resistance to blood flow through this system. Because earlier studies have been made only on forward perfusion of intact or isolated lungs(1-5) it seemed of interest to investi-

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gate the influence of these same mechanical factors during retrograde perfusion of the lung.

Methods. Adult mongrel dogs were anesthetized with intravenous 5% sodium pentobarbital (25-30 mg/kg) and were given intravenous heparin (3 mg/kg body weight). Following the administration of heparin, the femoral artery was cannulated and blood was collected for subsequent use in perfusion of the lung lobes. As soon as the dog was exsanguinated, a right thoracotomy was performed and both the right and left lower lobes were removed. In the resection of the lobes, care was taken to clamp the branches of the pulmonary arteries and veins with bulldog clamps in order to prevent air embolization. The lobes were then weighed in order that flow/gram of pulmonary tissue could be determined. In all of the experiments a cannula was placed in the bronchus and tied in place. Depending on the direction of the perfusion, a cannula was placed and tied into either the major pulmonary vein or artery. In those experiments in which wedge pressures were measured, a fine polyethylene catheter was wedged into the arterial or venous bed prior to the insertion of the perfusing catheter. Right and left lobes were alternated as to direction of the perfusion. The lobe was placed in a methyl methacrylate chamber and perfused with autologous blood through a system from which all glass had been excluded. The perfusing blood was passed through an alleviator shortly after leaving the Sigmamotor pump, in order to decrease the pulse pressure. At the time the perfusion was started, the lobe was ventilated with 100% oxygen at a pressure of 16 cm of water and a rate of 20-25 inflations per minute. Pressures were measured by Statham pressure transducers and recorded on a direct writing Sanborn apparatus. Perfusing rate of flow was determined by calibrating the system prior to the experiments by measuring delivered volume per minute with a stop watch and graduated vessel. Prior to, and at intervals during the experiment, zero pressure levels were obtained. Outflow pressures were measured by placing a fine polyethylene catheter (#090) 1-2 cm into the outflow vessel and suturing it in place in such a fashion that minimal constriction of the vessel was produced. Flow rates were varied from 45 cc/min to 500 cc/min. In general, a single rate of flow was maintained just long enough to allow the pressures to reach a steady state. The flow rate was increased progressively until obvious pulmonary edema, hemorrhage, and congestion occurred, with subsequent deterioration of the lobe. With outflow pressures above 25 mm Hg pulmonary edema and congestion occurred, and therefore only those observations with outflow pressures of 25 mm Hg or less are reported. Resistances were calculated employing the formula

$$R = \frac{\Delta P}{\text{Flow in cc/g/min}}$$

where ΔP is the difference between the perfusing pressure and outflow pressure.

Results. Tables I and II present the data

TABLE I. Venous Perfusions. Rate of flow (cc/min.).

Lobe #	Wt, g		45	100	200	300	400	500
1	34	R*	23.4	10.8	11.0	10.8		
		OP†	4.0	2.5	4.0	5.0		
		PP†	35.0	35.0	68.0	100.0		
2	32	R	16.9	15.3				
		OP	1.0	10.0				
		PP	25.0	58.0				
3	32	R	19.7	8.6	4.6	3.2		
		OP	5.0	3.0	9.0	17.0		
		PP	33.0	30.0	38.0	47.0		
4	35	R	19.5	10.1	6.6	5.6	5.3	5.1
		OP	0	1.0	2.0	2.0	1.0	1.0
		PP	25.0	30.0	40.0	50.0	62.0	75.0
5	46	R	4.1	6.0	3.2	2.8		
		OP	10.0	12.0	16.0	22.0		
		PP	14.0	25.0	30.0	40.0		
6	30	R	8.7	7.5	3.7	4.0		
		OP	12.0	15.0	25.0	25.0		
		PP	25.0	40.0	50.0	65.0		
7	31	R	12.4	8.4	6.2			
		OP	7.0	10.0	10.0			
		PP	25.0	37.0	50.0			
8	24	R	4.3	3.2				
		OP	12.0	22.0				
		PP	20.0	35.0				
9	25	R	7.2	7.5	4.8	2.5	2.4	1.8
		OP	12.0	10.0	12.0	25.0	22.0	25.0
		PP	25.0	40.0	50.0	55.0	60.0	60.0
Avg		R	12.9	8.6	5.7	4.8	3.9	3.5
		OP	7.0	9.5	11.1	16.0	11.5	13.0
		PP	25.2	36.7	46.6	59.5	61.0	67.5

* mm Hg/cc/g/min. † mm Hg.

R = Resistance. OP = Outflow pressure. PP = Perfusion pressure.

TABLE II. Arterial Perfusions.
Rate of flow (cc/min.).

Lobe #	Wt, g		45	100	200	300	400	500
1	34	R*	18.2	8.5	5.7	5.5	5.7	
		OP†	2.5	7.5	9.0	15.0	20.0	
		PP†	27.0	32.5	42.0	63.0	87.0	
2	27	R	19.8	14.9	10.0	7.7		
		OP	2.0	5.0	5.0	7.0		
		PP	35.0	61.0	79.0	92.0		
3	37	R	28.6	14.8	8.3	6.4	5.9	
		OP	2.5	3.5	5.0	8.0	10.0	
		PP	38.0	44.0	50.0	60.0	72.0	
4	35	R	11.7	12.9	6.6	4.4	3.9	3.4
		OP	0.0	0.0	1.0	1.0	1.0	1.0
		PP	15.0	37.0	39.0	39.0	45.0	50.0
5	66	R	8.8	6.6	4.7	4.0	3.9	3.7
		OP	5.0	10.0	11.0	12.0	13.0	12.0
		PP	11.0	20.0	25.0	30.0	37.0	40.0
6	46	R	30.6	18.3	12.4	8.9	9.0	8.9
		OP	0.0	0.0	1.0	4.0	2.0	2.0
		PP	30.0	40.0	55.0	62.0	80.0	100.0
7	31	R	11.7	9.3	7.1			
		OP	1.0	10.0	9.0			
		PP	18.0	40.0	55.0			
8	31	R	13.1	9.6	5.1	3.6	2.9	
		OP	11.0	14.0	15.0	20.0	22.0	
		PP	37.0	45.0	48.0	55.0	60.0	
9	29	R	4.5	6.4	4.1			
		OP	18.0	18.0	22.0			
		PP	25.0	40.0	50.0			
Avg		R	16.3	11.3	7.1	5.8	5.2	5.3
		OP	4.7	7.6	8.7	9.6	11.3	5.0
		PP	26.2	39.5	49.2	57.3	63.5	63.3

* mm Hg/cc/g/min. † mm Hg.
R = Resistance. OP = Outflow pressure. PP = Perfusion pressure.

from 9 pairs of lower lobes, in which corresponding numbers in the 2 tables represent lung lobes from one dog. It will be noted that the average perfusion pressure necessary to obtain a particular flow rate is not greatly different as between retrograde and forward perfusion. However, the average values of outflow pressure are higher in the retrograde perfusion situation and therefore the calculated resistances to flow between the points of measurement are somewhat higher for forward than for retrograde flow. It will also be noted that the resistance falls with increasing perfusion pressure with both forward and retrograde flow. Within limits of accuracy of measurement this was the case in all instances but two, in which outflow pressures were high at low flows. A comparison between outflow pressure levels and pulmonary vascular resistance indicates that maximal resistance was noted when outflow pressures were minimal. This correlation was observed with both retrograde perfusion and forward perfusion.

Discussion. It is of interest that the resistance to retrograde flow of blood in the pulmonary circuit is no greater, and may be somewhat less than that for forward flow within the small vessel bed. A further analysis of the relative importance of venous and arterial bed distention under pressure upon resistances to flow in the two segments must await more detailed analysis of pressure gradients within the vascular bed, including arterial wedge pressure measurements. It would be of interest to know the volume elasticity of arterial and venous segments and the relative effects of increasing the diameters of arterial and venous segments by pressure changes upon the resistances to blood flow through them.

Precise numerical data have not been obtained in this study, but it has been noted quite regularly in this study that pulmonary edema occurs sooner at a given high flow rate with retrograde than with forward flow. This would indicate, as would be predicted, that venules offer less resistance to distention than do arterioles and that therefore a larger fraction of the perfusion pressure obtains in the capillaries with retrograde than with forward flow. The occasional occurrence of low resistance at low flow rates could perhaps be related to variations in the magnitude of arterio-venous shunts(6,7) in one animal as compared to another.

Summary. Retrograde perfusion of the lung vessels of the dog is accomplished with no more resistance to flow than in forward flow. The calculated resistances in the smaller vessels is on the average less with retrograde than with forward flow. The resistance to flow in either direction diminishes with increased perfusion pressure. Gross observation indicates a more rapid production of lung edema at high perfusion rates with retrograde than with forward perfusion.

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Methods for Studying Lymphatic Function in Intact Man Utilizing Au^{198}.* (23914)

HAROLD H. SAGE AND BENJAMIN V. GOZUN (Introduced by J. H. Mulholland)
Guggenheim Institute for Dental Research, New York University College of Medicine

Methods have been devised for studying functional patterns, dynamics and quantitative particle pickup by intact lymphatics and lymph nodes under various conditions. Previous methods using intracutaneous injection of particulate dyes, as that of Hudack and McMaster(1), have demonstrated the pattern of fine superficial cutaneous lymphatics in various experimental and clinical states. Demonstration of deeper lymphatic channels and lymph nodes by pickup of stained particles or radioactive gold has required operative exposure of lymph-bearing tissues and lymph nodes(2,3). The methods to be described require no operation and provide graphic records of lymph node pickup, and quantitative measurements of such pickup. Thus, serial physiologic and diagnostic studies can be performed.

Method. Pictorial pattern of lymph node pickup is obtained by local injection of radioactive gold and the use of a scintiscanner. Similar Lymphatic Scintigrams were first obtained in dogs(4). Injection of Au^{198} into various sites in head and neck precedes continuous or interval scintiscanner recording of the pickup by deep lymphatics and lymph nodes. Since the half-life of radioactive gold is 2.69 days, speed of disappearance from site of injection and later distribution in the lymphatic system can be recorded. Lymphatic scintigrams have now been obtained in both upper and lower extremities in intact humans. Fifty to 100 microcuries of radioactive gold are injected into subcutaneous tissues of calf of leg. Deposition in femoral and inguinal nodes within 10 minutes to an hour can be detected under normal conditions. The first node (Fig. 1, part a.) to be outlined is usually in the femoral triangle about one to two inches below the inguinal ligament. The pictorial pattern obtained can be varied by altering the sensitivity and kinetics of the scintiscanner. This counter moves automatically across and up and down the field at varied speeds which increase or decrease the concentration of recorded dots. Thirty to 60 minutes may be required to scan the area

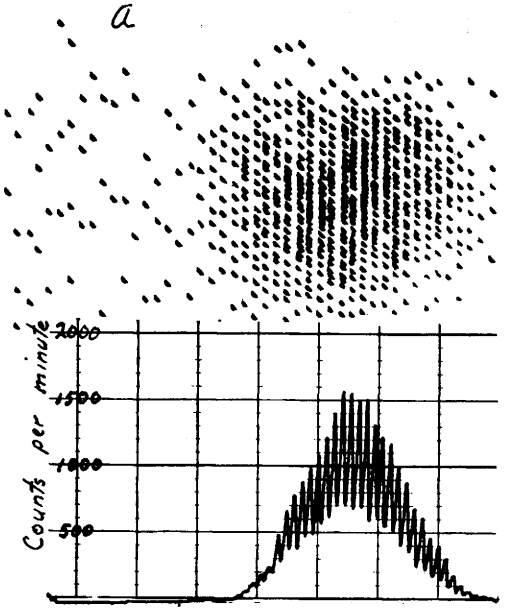

FIG. 1. a. (top) Lymphatic scintogram of femoral region 24 hr after inj. of 100 microcuries of Au^{198} inj. into subcut. tissues of calf. b. (bottom) Count rate meter graph run simultaneously and coordinately with 1-a.

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