TABLE I. Lack of Sparing Effect of Vit. A Acid on Vit. A in Vaginal Smear Assay.

Dose				
Vit. A (μg)	15	15	30	30
Vit. A acid (μg)*	—	50	—	100
Response (days)	7.6	8.3	9.1	8.9

* Administered for first 5 days only.

group Vit. A acid was 8% as active as Vit. A. This is similar to estimates made by the growth assay(2) but differs from the results of Boguth *et al.*(3) who found Vit. A and its acid equal in potency. The technic of Boguth *et al.* required much larger doses and there is some indication that the estimated potency of Vit. A acid varies with the size of the dose, *e.g.*, the slope of the response curve of Vit. A acid was greater than that of Vit. A. The amount of Vit. A required to cure all deficient rats in a group was 6 times that required to cure any, while the same response could be obtained by doubling the smallest effective dose of Vit. A acid. Similarly Matschiner and Doisy(8) found that increasing a dose of Vit. A acid 10-fold had a more marked influence on Vit. K deficiency than did a similar increase in Vit. A. In this respect Vit. A acid differs from other forms of Vit. A, such as the *cis* isomers, which have low biological potency but a response curve of the same slope as the all-*trans* form. Perhaps this characteristic of Vit. A acid is related to the fact that excess amounts cannot be stored but are quickly metabolized.

The 2-*cis* and 6-*cis* isomers of Vit. A acid, for which potencies have not previously been reported, were 50% and 15% as active respectively as the all-*trans* isomer. This relationship resembles that of the same isomers of Vit. A and suggests features common to both in the metabolic pathways of Vit. A and Vit. A acid. This hypothesis is difficult to reconcile, however, with the lack of sparing action of Vit. A acid for Vit. A which has been demonstrated by 3 methods, disappearance of liver stores(5), appearance of night-blindness(5) and by the vaginal smear assay.

Summary. The biological potency of Vit. A acid was measured by a modified vaginal smear assay and found to be 8% that of Vit. A. The results suggested that the potency of Vit. A acid, relative to that of Vit. A, may vary with the dosing level used. 2-*cis* and 6-*cis* Vit. A acid were 50% and 15% respectively as potent as the all-*trans* form. Vit. A was not spared by daily doses of Vit. A acid.

The author wishes to acknowledge the technical assistance of Mr. C. J. Desologes and the generosity of Dr. Grove Baxter of Distillation Products Industries for samples of the *cis* isomers of vitamin A acid.

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Received August 27, 1962. P.S.E.B.M., 1962, v111.

Arterial Blood Flow During Elevated Intrapulmonary and Intra-Abdominal Pressures. (27870)

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It is now generally recognized that cardiac output decreases in man(1,2) and animals (3,4) during continuous positive pressure breathing (CPPB); however, mainly indirect methods such as skin or muscle temperature (5,6,7), plethysmography(8,9) and local ab-

sorption of radioactive sodium(10) have been used to determine reductions in peripheral blood flow. Herrick *et al.*(11) and later Beecher *et al.*(12), using electronic flowmeters on cannulated vessels, observed marked to inconsistent decreases in arterial blood flow of anesthetized dogs during extremely high (60 mm Hg) or low (7 mm Hg) intrapulmonary pressures. Since peripheral vasoconstriction, as well as abdominal muscle tone(13), play an important role in the restoration of depressed arterial pressures observed during CPPB, a series of experiments was designed to ascertain carotid and femoral arterial blood flow, pressure and resistance at various levels of elevated CPPB, and further, to compare these findings with those observed during elevated intra-abdominal pressures (AbPB).

Materials and methods. Twenty-one male mongrel dogs weighing 14-18 kg were anesthetized with sodium pentobarbital (25 mg/kg), prior to tracheotomy. As required, supplemental doses of the anesthetic were administered during the experiment to maintain the proper level of anesthesia. After isolating the left carotid (11 dogs) and femoral (10 dogs) arteries, the animals were heparinized and polyethylene cannulae of appropriate sizes inserted into the proximal and distal ends of the vessels. As previously described (14), the ends of the cannulae were connected to a T-tube and electromagnetic flow probe from which lateral pressures (Statham Transducer) and blood flow were monitored, respectively, on a Grass Polygraph. A positive pressure regulator, connected to a compressed air line, was attached to the cannulated trachea of 7 carotid and 6 femoral preparations. In the remaining 8 animals (4 carotid, 4 femoral) an aluminum cannula coupled to the pressure regulator was tied securely into the peritoneal cavity through a stab wound in the abdominal wall. Pressures of 3, 7, 10, 14, 18 and 21 mm Hg were randomly applied to either the trachea or peritoneal cavity and maintained for 5 minutes. Sufficient time elapsed prior to the application of a new pressure for all circulatory parameters to stabilize.

Results. The relationships between mean arterial pressure and blood flow in the carotid and femoral arteries as a function of increasing CPPB are presented in Table I. Immediately upon the application of CPPB (On) blood pressures progressively decreased until they were inversely proportional to increasing CPPB. Following these primary decreases, femoral arterial pressures rapidly returned towards control levels during the maintenance of 3-21 mm Hg CPPB, whereas carotid pressures which recovered approximately 5-25%, were significantly lower ($P<.01$) than control and femoral pressures during 10-21 mm Hg CPPB. The removal of CPPB (Off) caused marked elevations from maintenance levels of all arterial pressures; however only femoral pressures at 14-21 mm Hg CPPB were markedly increased above pre-pressure breathing levels prior to returning to control.

The initial application of increasing CPPB caused pronounced reductions in arterial blood flows concomitantly with progressive diminutions in mean arterial pressures. Vascular resistance at this time (On) promptly increased since blood flow decreased more rapidly than mean pressure. Subsequently, blood flows although recovering 5-15% during the maintenance of 7-21 mm Hg CPPB, remained significantly depressed from control levels ($P<.01$) and inversely proportional to increasing CPPB. There were no significant differences between carotid and femoral blood flows at this time. Femoral vascular resistance was significantly elevated ($P<.01$) during the maintenance of 10-21 mm Hg CPPB, since blood flow remained depressed while mean arterial pressure returned to essentially control levels. On the other hand, carotid blood flow and pressure decreased at approximately proportional rates resulting in only slight increases in resistance which were significantly lower ($P<.01$) than femoral resistance at 10-21 mm Hg CPPB but not from their respective controls.

In general the removal of high intrapulmonary pressures produced greater elevations in arterial blood flow than pressure, resulting in resistance values which were never greater than those observed during the maintenance of positive pressure and only higher ($P>.30$)

TABLE I. Alterations in Arterial Pressure, Flow and Resistance During 5 Minutes of CPPB and AbPB

Pressure mm Hg	Intrapulmonary pressure — CPPB — Femoral On	Femoral During	Femoral Off	Carotid On	Carotid During	Carotid Off	Intra-abdominal pressure — AbPB — Femoral On	Femoral During	Femoral Off	Carotid On	Carotid During	Carotid Off
					Mean Arterial Pressure							
3	94 ± 3*	99 ± 3	100 ± 2	93 ± 2	97 ± 1	99 ± 1	89 ± 4	100 ± 1	104 ± 2	97 ± 1	98 ± 1	99 ± 1
7	87 ± 2	99 ± 1	103 ± 2	80 ± 4	95 ± 1	104 ± 4	92 ± 3	96 ± 2	107 ± 3	92 ± 2	97 ± 1	100 ± 3
10	72 ± 6	102 ± 1	111 ± 5	67 ± 5	86 ± 3	100 ± 5	85 ± 4	94 ± 2	107 ± 3	86 ± 1	97 ± 1	104 ± 2
14	69 ± 4	105 ± 2	120 ± 8	59 ± 6	86 ± 3	106 ± 6	83 ± 4	92 ± 2	105 ± 2	82 ± 5	97 ± 1	106 ± 2
18	64 ± 6	103 ± 1	123 ± 7	48 ± 5	72 ± 5	97 ± 6	76 ± 3	95 ± 3	115 ± 4	83 ± 3	99 ± 1	108 ± 2
21	51 ± 3	99 ± 3	127 ± 10	42 ± 4	63 ± 5	96 ± 8	75 ± 3	95 ± 2	105 ± 6	83 ± 5	99 ± 1	108 ± 1
					Arterial Blood Flow							
3	90 ± 3	94 ± 2	105 ± 3	94 ± 2	98 ± 1	101 ± 2	99 ± 1	101 ± 1	107 ± 7	99 ± 1	97 ± 2	103 ± 3
7	81 ± 4	80 ± 3	117 ± 8	76 ± 1	87 ± 1	122 ± 5	85 ± 6	86 ± 1	105 ± 9	95 ± 2	96 ± 1	102 ± 2
10	57 ± 6	71 ± 3	112 ± 13	62 ± 4	74 ± 2	121 ± 4	89 ± 5	86 ± 5	124 ± 10	94 ± 3	93 ± 2	102 ± 3
14	54 ± 5	68 ± 3	128 ± 11	57 ± 3	69 ± 2	120 ± 5	84 ± 4	80 ± 4	117 ± 8	93 ± 3	92 ± 2	107 ± 4
18	48 ± 3	52 ± 4	152 ± 20	41 ± 5	53 ± 4	98 ± 5	93 ± 5	74 ± 4	109 ± 4	88 ± 2	87 ± 2	99 ± 3
21	30 ± 4	42 ± 4	137 ± 16	31 ± 3	45 ± 2	113 ± 5	76 ± 9	71 ± 5	142 ± 18	92 ± 5	85 ± 2	94 ± 5
					Vascular Resistance†							
3	105 ± 5	106 ± 2	95 ± 1	98 ± 2	99 ± 1	98 ± 2	90 ± 5	99 ± 1	99 ± 4	98 ± 2	100 ± 1	97 ± 2
7	109 ± 5	126 ± 4	90 ± 6	105 ± 5	109 ± 2	86 ± 2	102 ± 5	112 ± 3	105 ± 9	97 ± 2	96 ± 2	98 ± 3
10	121 ± 5	148 ± 10	112 ± 22	102 ± 9	110 ± 6	78 ± 6	95 ± 2	113 ± 6	89 ± 7	91 ± 3	94 ± 2	102 ± 2
14	133 ± 10	164 ± 9	102 ± 13	103 ± 9	127 ± 7	90 ± 8	100 ± 4	117 ± 4	90 ± 5	87 ± 4	92 ± 2	101 ± 5
18	136 ± 10	212 ± 15	93 ± 18	125 ± 15	147 ± 9	98 ± 5	93 ± 3	132 ± 6	112 ± 11	94 ± 2	95 ± 3	109 ± 2
21	180 ± 18	285 ± 40	105 ± 23	156 ± 32	142 ± 9	86 ± 7	91 ± 4	148 ± 11	79 ± 11	91 ± 3	95 ± 2	116 ± 6

* Mean % of control ± standard error.

† Mean arterial pressure/flow.

than control in 3 experiments (Table I).

All levels of AbPB did not materially affect carotid or femoral arterial pressures during the 5-minute experimental period, although transitory depressions and elevations were noted during the application and removal of AbPB respectively (Table I). Femoral blood flow was significantly depressed from control ($P<.01$) during the maintenance of 7-21 mm Hg AbPB causing vascular resistance to gradually increase 42% above control. On the other hand, carotid vascular resistance remained essentially unchanged, since blood flow diminished markedly only at the highest abdominal pressure (21 mm Hg). The removal of AbPB caused variable alterations in flow and resistance which rapidly subsided to normal levels.

Discussion. Many investigators have observed a primary decrease in arterial pressure immediately upon application of CPPB with a subsequent return towards control pressure depending on the level of CPPB(13,15,16, 17). The results presented herein confirm these earlier observations; however, as previously reported(15) femoral arterial pressures returned towards control levels within one minute of 3-21 mm Hg CPPB, whereas carotid arterial pressures remained at depressed levels throughout CPPB. In anesthetized animals, the precipitous fall in arterial pressure is accompanied by a period of apnea, diminished heart rate and elevated central venous pressure(14,15) which undoubtedly impaired venous return and ultimately cardiac output. Therefore it is not surprising that arterial blood flow was depressed during elevated intrapulmonary pressures. The findings reported herein are of much interest in that marked differences occurred between the carotid and femoral arteries. In the former artery vascular resistance increased proportionately with increasing levels of CPPB, whereas in the latter artery resistance remained essentially unaltered. By comparing carotid arterial distribution with that of the femoral artery, the former distributed to fewer muscles and supplying more vital structures, the importance of peripheral vasoconstriction to maintain blood supply to vital structure like the brain can be demonstrated. It is well known that whenever the effective circulating volume is diminished, as it is during CPPB(19), the remaining circulatory volume is shunted to supply the most vital organs. Thus resistance does not increase in the structures supplied by the carotid artery else it would further diminish circulation to this area. Teleologically one can assume that since vascular resistance markedly increased in the extremities it was to shunt blood away from non-vital structures.

The elevation in blood pressure (overshoot) upon removal of CPPB has been attributed to a sustained increase in peripheral resistance observed during CPPB or a further increase upon its removal(12,16,20). In our experiments it was noted that although arterial pressures increased at this time, blood flow increased to a greater extent causing vascular resistance to decline from elevated pressure breathing levels. Since vascular resistance was not increased over and above CPPB levels, the contribution of vasomotor tone to the overshoot was certainly not greater than during the maintenance of CPPB. Thus the data suggest that the overshoot in arterial pressure and flow is caused primarily by an increased stroke volume(15) resulting from accelerated venous return(18) after removal of the cardiac tamponade(21).

The observations on AbPB are consistent with those of others(15,22) who reported that elevated intra-abdominal pressures do not affect arterial pressures excepting for slight diminutions and elevations observed during its application and removal, respectively. It has been postulated that the abdominal veins are emptied during the initial onset of AbPB and its removal is accompanied by a release of the blockade to venous flow from the lower extremities(15). The resulting momentary fluctuations in venous return are suggested by the observed decrease and subsequent increase in carotid and femoral arterial blood flows during application and removal of AbPB. The maintenance of AbPB for 5 minutes, although not affecting carotid and femoral arterial pressures, caused a significant decrease in femoral blood flow. Previous experiments(15) illustrated

that AbPB caused greater increases in inferior vena caval pressure than femoral venous pressure thus impairing circulation through the limb. On the other hand, the diaphragm which is displaced headwards prevents a rise in thoracic venous pressure and allows blood to circulate essentially unimpeded.

Summary. Anesthetized dogs were subjected to 3-21 mm Hg CPPB or AbPB. Carotid and femoral arterial blood flow and mean carotid pressure decreased inversely proportional to increasing CPPB while femoral pressure remained essentially unaltered. Thus vascular resistance was significantly elevated only in the femoral circulation. In general, since all levels of AbPB were without effect except for the slight depression in femoral flow, the data suggest that elevations in abdominal pressure which occur during CPPB do not play a significant role in the restoration of circulatory parameters.

The technical assistance of W. Kadetz and E. F. Robbins and the advice and criticism of Dr. J. P. Marbarger are greatly appreciated.

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Received August 29, 1962. P.S.E.B.M., 1962, v111.

Influence of Foster-Nursing on Virus-Induced and Spontaneous Leukemia in Mice. (27871)

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Preliminary results have been reported of a study of the congenital transmission of the leukemogenic virus of Moloney (MLV) in certain inbred strains of mice(1). Transmission of virus occurred through the maternal line in 3 C3H sublines, 2 low-leukemic (Gs and Lw) and one high-leukemic (Fg). Offspring born to non-infected females mated with MLV-infected males, however, did not develop a higher frequency or earlier disease than controls observed concomitantly. The most effective route of transfer in the maternal line was through the mother's milk. Transmission of MLV during the prenatal period was found to be relatively ineffective.

The present report is an extension of the