that the parenteral administration of various mast-cell dischargers following an intravenous injection of agar induces a type of anaphylactoid purpura. This syndrome is characterized by thrombohemorrhagic lesions in the anaphylactoid shock organs, especially the snout, paws and sometimes the root of the tail.

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Systemic and Coronary Hemodynamic Effects of Pseudoephedrine.* (29937)

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Pseudoephedrine (Sudafed®) has been promoted as a nasal and tracheo-bronchial decongestant because it has been found to have less effect on the blood pressure than its optical levo-isomer ephedrine(1-4). This compound, dextro-ephedrine (1-phenyl, 2-methylamine propanol-1-hydrochloride) is reported to cause approximately one-half as much elevation in blood pressure as ephedrine(2-3) and some differences in pharmacologic properties have been reported(5). Further information concerning its effect on the cardiovascular system in general, however, is limited and the drug was accorded no significance in a recent extensive review of the circulatory effects of sympathomimetic amines (6).

Materials and methods. The present study was done in 11 anesthetized mongrel dogs varying in weight between 15 and 30 kg with an average weight of 23.2 kg. These dogs were anesthetized by administration of 3 mg/kg of morphine sulfate subcutaneously followed one hour later by 0.25 ml/kg of veterinary pentobarbital and dial-urethane‡ intravenously. In the ensuing hour after establishment of anesthesia cardiac catheters were inserted through the jugular veins and manipulated fluoroscopically into the pulmonary artery, coronary sinus, and right atrium and a needle was placed percutaneously in the femoral artery for recording of pressures and drawing of blood specimens. Pressures were recorded by way of Statham strain gauge pressure transducers on a Sanborn 4-channel Poly-Viso. Mean pressures were determined by electrical damping. Expired air was collected through an endotracheal tube and low resistance large-bore tubing in a Tissot spirometer. Expired air was analyzed for oxygen and carbon dioxide by the method of Scholander. Blood specimens were analyzed by the Van Slyke-Neill manometric method. Analyses for arterial blood oxygen content were required to check within 0.2 ml. Cardiac output was measured by the direct Fick principle and coronary blood flow by the nitrous oxide saturation method utilizing the partition coefficient one. Cardiac work was calculated by the usual Starling formula.

After control observations had been made, pseudoephedrine was infused at a rate of one or two mg/kg body weight/minute. Approximately 7 minutes after onset of the drug in-

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‡ Dial-urethane contains Dial 100 mg/ml, monoethylurea 400 mg/ml, and urethane 400 mg/ml. Veterinary pentobarbital contains 60 mg/ml of pentobarbital.

TABLE I. Effects of Pseudoephedrine.

Parameter	Control	Drug	% change	SEM diff.*	P value
Heart rate, beats/min	74	69	− 6.8	1.923	<.05
Mean art. blood pressure, mm Hg	122	134	+ 9.8	2.992	<.01
Mean pulm. art. blood pressure, mm Hg	15	16	+ 6.7	.447	<.05
Mean rt. atrial blood pressure, mm Hg	4.8	4.9	+ 2.1	.162	<.6
Oxygen consumption, ml/min	118	118	—	—	—
Body respiratory quotient	.87	.86	− 1.2	.016	<.6
Arterial oxygen content, ml/100 ml blood	17.0	17.5	+ 2.9	.324	<.2
Cor. sinus oxygen content, ml/100 ml blood	4.9	6.6	+34.7	.632	<.05
Arterial hematocrit,%	44	46	+ 4.5	.625	<.01
Arterial hemoglobin, g/100 ml	14.2	14.7	+ 3.5	.199	<.1
Cardiac output, L./min	2.8	2.7	− 3.6	.237	>.9
Left ventricular work, kg M/min	4.6	5.2	+13.0	.418	<.2
Right ventricular work, kg M/min	.6	.6	—	—	—
Total peripheral resistance, cgs units	3950	4310	+ 9.1	225.686	<.2
Total pulmonary resistance, cgs units	500	537	+ 7.4	28.393	<.3
Coronary blood flow, ml/100 g/min	81	103	+27.2	14.763	<.2
Left vent. oxygen usage, ml/100 g/min	9.5	11.7	+23.2	1.633	<.3
Coronary vascular resistance, units	1.54	1.45	− 5.8	.092	<.4
Cardiac respiratory quotient	.89	.86	− 3.4	.013	<.05
Index of efficiency, LVW ÷ LVO_2 usage	.50	.51	+ 2.0	.435	.0

* Standard error of mean difference.

fusion, the second determination of cardiac output and coronary blood flow was begun. Since the response to these 2 doses did not appear to be basically different, all of the data were pooled for final statistical analysis by use of the t-test. The results are summarized in Table I.

Results. During the administration of pseudoephedrine there was a slight, but statistically significant decrease in cardiac rate, accompanied by a modest but significant increase in blood pressure in the systemic and pulmonary arteries. The right atrial pressure did not change. Neither respiratory volume, body oxygen consumption nor CO_2 elimination changed and the respiratory quotient was constant. A significant increase occurred in arterial hematocrit and simultaneously a slight but insignificant increase occurred in hemoglobin and arterial oxygen content. The arterio-venous oxygen difference did not change. There were significant decreases in arterial and mixed venous carbon dioxide content; however, this occurs so commonly in dogs anesthetized by this method that no significance should be attributed to this change. The coronary sinus oxygen content was significantly increased, but the arterial-coronary sinus oxygen difference did not change significantly. The cardiac respiratory quotient decreased. Cardiac output was unchanged. Left ventricular work increased slightly, but not significantly, and right ventricular work was constant. Total peripheral and pulmonary resistance increased slightly, but not significantly. There was no significant increase in coronary blood flow or in myocardial oxygen consumption, although both tended to rise variably. The index of efficiency, which relates myocardial oxygen consumption to left ventricular work was not altered, and the stroke volume was constant.

Discussion. Preceding studies have indicated that pseudoephedrine (Sudafed®) has less hemodynamic effect than does ephedrine itself(1-5). The present essentially negative study of pseudoephedrine would tend to confirm these observations and extend them to further parameters than have been investigated previously. It would appear that, in the doses administered to these animals, some vasoconstriction occurred since there were slight but insignificant increases in the peripheral and pulmonary vascular resistances. This was accompanied by a mild increase in the mean systemic arterial blood pressure, and a reduction in cardiac rate. Presumably the decrease in cardiac rate is related reflexly to the increase in systemic arterial pressure. It should be noted that neither the total body oxygen consumption nor the left ventricular oxygen consumption

were significantly changed. An increase occurred in arterial hematocrit as may occur with administration of sympathicomimetic amines. This was accompanied by a slight rise in the hemoglobin and in the oxygen content of arterial, mixed venous and coronary sinus blood. These increases in oxygen content were variable, however, and statistical significance was reached only by the increase in coronary sinus oxygen content.

It is desirable for an agent used primarily as a local vasoconstrictor in the mucous membranes of the nasopharynx and the tracheobronchial tree to have minimal cardiovascular effects. According to the present studies pseudoephedrine hydrochloride would seem to fulfill this portion of the desirable criteria.

Conclusions. 1. Pseudoephedrine hydrochloride has been administered to a group of anesthetized mongrel dogs in a dose of 1 or 2 mg/kg/minute. Systemic and coronary hemodynamics have been determined before and during its administration. 2. A minor but consistent increase occurred in systemic arterial pressure accompanied by a decrease in cardiac rate. 3. There was a slight but significant increase in hematocrit and in coronary sinus oxygen content. 4. No significant change occurred in cardiac output, coronary blood flow or other measured parameters, consequently the hemodynamic effects may be considered to be minimal.

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Heterozygosity and Homozygosity in von Willebrand's Disease.* (29938)

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Biosynthesis of the antihemophilic factor (AHF, F. VIII) in humans is clearly under the control of at least 2 genetic loci. Mutation at a locus on the X-chromosome produces classical hemophilia A, while mutation at an autosomal locus results in von Willebrand's disease (v.W.d.). In both disorders the plasma AHF activity is reduced(1). The genetic situation is complex, however, because a type of *non-reciprocal* "complementation" is observed when the mutant phenotypes are cross-transfused. Briefly, a transfusion of hemophilia A plasma apparently stimulates persons with v.W.d. to synthesize AHF, while a transfusion of v.W.d. plasma has no effect on plasma AHF activity of persons with hemophilia A(2).

The descriptions of families with v.W.d. seem to define only a single abnormal phenotype(1). The affected members appear to form a continuum, although they vary somewhat in severity of symptoms and AHF levels. Recently, we have encountered a family with v.W.d. which contains 2 mutant phenotypes responding quite differently to transfusion of hemophilia A plasma, the test now regarded as the hallmark of v.W.d.(1). The genetic relations within this family suggest that the mild bleeders are heterozygotes and the severe ones homozygotes. The differences between the abnormal phenotypes are of considerable clinical and genetic interest, but they are important chiefly because of the light they shed on the alternative hypotheses of AHF biosynthesis. In short, the differences appear to exclude the "regulatory" hypothesis but not the "combining subunit"

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