The Effects of Hemolyzed Blood on Pulmonary and Systemic Arterial Pressure and Heart Rate of the Dog

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ABSTRACT

The injection of hemolyzed blood into the venous system of the dog produced a rise in the pulmonary arterial pressure and a fall in the systemic arterial pressure. There were variable changes in the heart rate. Comparison with serotonin injections indicated that the above responses were produced by factors other than serotonin.

RÉSUMÉ

L'injection intra-veineuse de sang hémolysé à des chiens produisit une élévation de la pression artérielle pulmonaire et une chute de la pression artérielle systémique. Le rythme cardiaque subit aussi des changements variables. Des injections comparatives de sérotonine révélèrent que les observations énumérées ci-haut résultaient de facteurs autres que la sérotonine.

INTRODUCTION

As early as 1870 it had been suggested that hemoglobin from hemolyzed blood was toxic when injected systemically (1). Brodie reported in 1900 that the intravenous injection of homologous and heterologous sera produced a fall in arterial pressure (2). Janeway *et al* isolated an active systemic and pulmonary pressor substance from platelets that was identified by Rapport as serotonin (5, 7). In 1944, Gilding *et al* reported an active agent in serum in addition to serotonin (4). A study conducted in 1958 revealed that an endotoxin also produced a rise in pulmonary arterial pressure (6).

The purpose of this study was to determine the effects in dogs of hemolyzed blood on pulmonary and systemic arterial pressures and heart rate. The responses produced by the injection of hemolyzed blood were compared to those produced by the injection of prepared serotonin standards.

MATERIALS AND METHODS

Ten mature mongrel dogs of both sexes weighing between 10 and 20 kilograms were used in the study. Each dog was fasted 24 hours. Anesthesia was induced with thiamylal sodium[1] and maintained with methoxyflurane[2] using a gas anesthetic machine.[3] Systemic arterial blood pressure was monitored by catheterization of the right common carotid artery and pulmonary arterial pressure by catheterization of the main pulmonary artery via the right jugular vein. Injections of hemolyzed blood and serotonin were administered through a catheter positioned in the femoral vein. Strain

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[1]Surital, Parke, Davis and Company, Detroit, Michigan.

[2]Metofane, Pitman-Moore Company, Indianapolis, Indiana.

[3]Airco, Ohio Medical Products, Madison, Wisconsin.

gauge tranducers were used[4] and recordings made on a multichannel oscillograph.[5] In addition to systemic and pulmonary arterial pressures, electrocardiograms and cardiotachograms were monitored.

Blood samples were taken from each dog eight to 24 hours prior to use and each sample was analyzed for serotonin content(12). After each dog had been anesthetized and the catheters positioned 5 ml of blood were collected from the femoral vein and hemolyzed with 5 ml of distilled water. Each hemolyzed sample was held for 20 minutes prior to injection.

Hemolyzed blood and serotonin were administered according to the following schedule:

1. Five sequential 10 ml intravenous injections of autologous hemolyzed blood.
2. Three sequential, 10 ml intravenous injections of serotonin at doses of 5, 50 and 100 μg, respectively.

RESULTS

Response to Hemolyzed Autologous Blood

The rapid injection of 5 ml of autologous hemolyzed blood given over a total of 50 injections in ten dogs produced an average increase in pulmonary arterial pressure of 4.9 mm Hg (Table I). Increases in pulmonary arterial pressure were accompanied by decreases in left carotid arterial pressure averaging 18.1 mm Hg (Table II). An increase in both systolic and diastolic pressures characterized the pulmonary pressure rise, whereas the systemic decrease resulted mainly from a fall in the diastolic pressure.

Initial injections of hemolyzed blood ordinarily produced the greatest pressure drop. When injections were repeated at short intervals (ten minutes) responses were not as great as those produced by the first injection. The pulmonary arterial pressure increased an average of 8.5 mm Hg and the carotid arterial pressure decreased an average of 35.5 mm Hg in response to the first injection. These values represent changes of 80% and 31%, respectively. The pulmonary arterial pressure usually returned to preinjection values within approximately two minutes and the carotid arterial within three minutes (Fig. 1).

Changes in heart rate from injection of hemolyzed blood were highly variable and inconsistent. Both increases and decreases in heart rate were observed. In four of the ten dogs, changes in the ECG indicated the presence of paroxysmal tachycardia immediately following the injection of hemolyzed blood.

Response to Serotonin

The average serotonin content of the hemolyzed blood collected from the dogs was 2.80 μg (1.25-5.65 μg) per 5 ml. Injections of 5 μg, 50 μg and 100 μg of serotonin into the femoral vein resulted in an average increase of 0.3 mm Hg, 2.6 mm Hg and 5.4 mm Hg, respectively, in pulmonary arterial pressure. Observed changes in the systemic pressure for the same concentrations of serotonin were 1.5 mm Hg increase, 1.0 mm Hg decrease and 1.5 mm Hg increase, respectively.

DISCUSSION

The injection of hemolyzed blood into the venous system of the dog produced a rise in the pulmonary arterial pressure and a fall in the systemic arterial pressure. This was accompanied by a change in the heart rate which varied with injections, either increasing or decreasing.

It was also noted that when the injections were repeated the responses were not as great as those produced by the first injection ($P < 0.01$ for pulmonary arterial pressure and for systemic arterial pressure). The first injection produced a response in both parameters greater than twice the responses to the succeeding four

[4]Stratham, P23Db & P23BB, Hato Rey, Puerto Rico.

[5]Brush MK 200, Brush Instruments, Div. of Gould, Inc., Cleveland, Ohio.

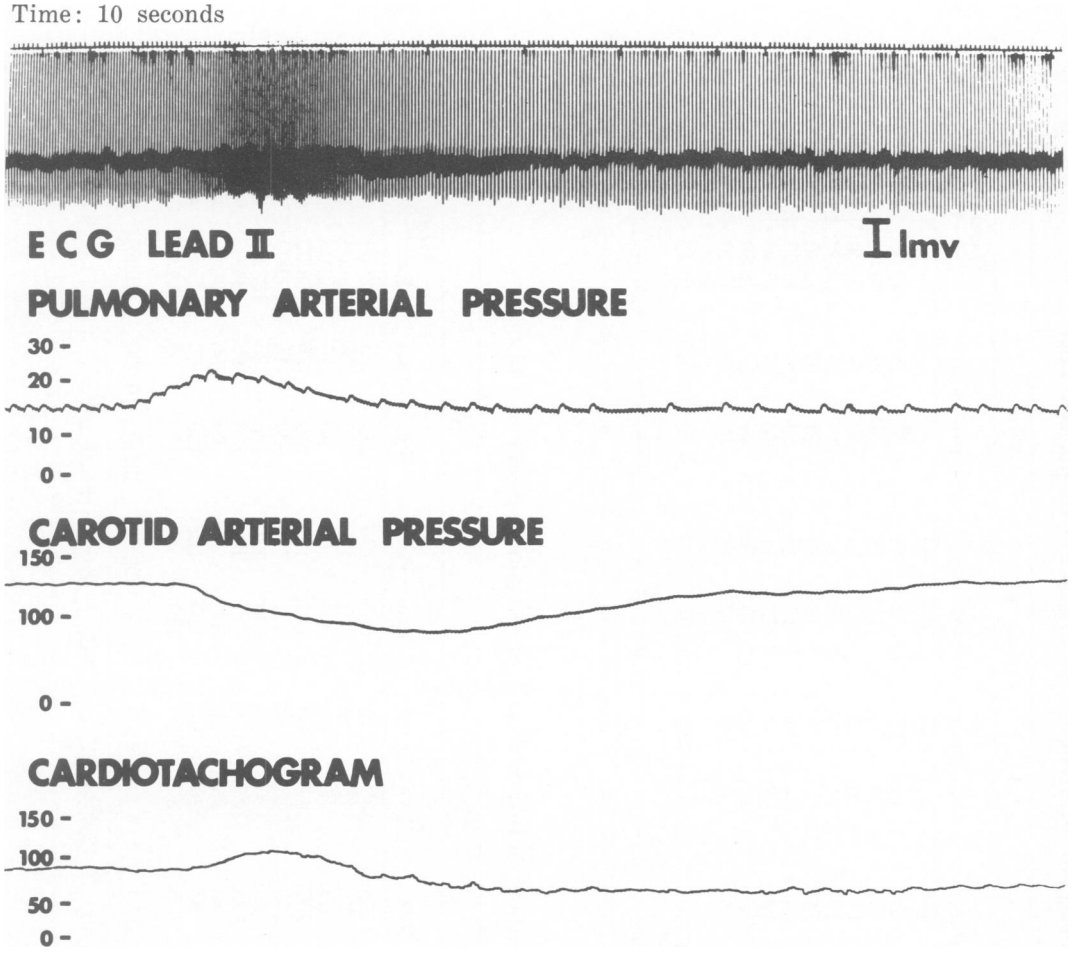

Fig. 1. Electrocardiogram, pulmonary arterial pressure, carotid arterial pressure and cardiotachogram from a dog following an initial 10 ml intravenous injection of autologous hemolyzed blood.

injections. It is thought that perhaps this could result from tachyphylaxis.

It has been suggested that these responses are due to serotonin liberated during hemolysis (3, 7, 9). The serotonin levels of hemolyzed blood used in this experiment were found to average 0.56 μg/ml or 2.80 μg/5 ml. When 5 μg of serotonin were given to these dogs no significant response was produced. The injection of 100 μg of serotonin was needed to elicit a pulmonary arterial response similar to that of the 5 ml of hemolyzed blood. Serotonin produced essentially no change in the systemic pressure. Thus the responses to injections of hemolyzed blood must have been produced by factors other than serotonin or by other substances acting in conjunction with serotonin (10, 11).

An amount of fibrin may be formed during the hemolysis of blood which could be said to produce pulmonary embolism and a consequent increase in pulmonary arterial pressure. However, it has been shown that the pulmonary effect of hemolyzed blood can be reversed by the injection of isoprenaline (11). Moreover, an increase in pulmonary arterial pressure due to mechanical blockage would likely last longer than the usual two minute response to injection.

Hemolyzed blood can be present in the circulation due to several mechanisms and the clinical implications of this may be significant. For example it has been shown that the hemolysis of blood is associated with use of heart-lung machines (13, 14). Likewise, hemolysis due to turbulence caused by patent ductus arterious and ventricular septal defects has been suggested

TABLE I. Pulmonary Arterial Pressure Response (mm Hg) in Dogs to Intravenous 5 ml Aliquots of Hemolyzed Blood

	1		2		3		4		5				
Dog	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Mean Pre	Mean Post	Mean Diff.
1	11	21	12	12	14	16	16	27	18	26	14.20	20.40	6.20
2	11	24	11	13	11	12	12	13	13	16	11.60	15.60	4.00
3	7	15	9	15	10	15	11	15	11	16	9.60	15.20	5.60
4	7	17	10	14	10	17	10	13	10	11	9.40	14.40	5.00
5	11	17	12	17	14	18	13	17	14	20	12.80	17.80	5.00
6	10	12	13	14	13	15	13	13	13	16	12.40	14.00	1.60
7	14	28	14	23	14	14	13	13	13	20	13.60	19.60	6.00
8	12	17	12	19	12	14	12	21	14	15	12.40	17.20	4.80
9	10	20	12	16	11	13	15	16	16	17	12.80	16.40	3.60
10	13	20	13	16	16	19	17	28	18	27	15.40	22.00	6.60
Mean	10.60	19.10	11.80	15.90	12.50	15.30	13.20	17.60	14.00	18.40	12.42	17.26	4.84
Mean diff. with confidence limits[a]	8.50 ± 2.62		4.10 ± 1.98		2.80 ± 1.02		4.40 ± 3.13		4.40 ± 2.16		4.84 ± 1.06		

[a] $P > 0.05$

TABLE II. Pulmonary Arterial Pressure Response (mm Hg) in Dogs to Intravenous 5 ml Aliquots of Hemolyzed Blood

	1		2		3		4		5				
Dog	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Mean Pre	Mean Post	Mean Diff.
1	125	90	125	125	130	140	140	110	140	125	132.00	118.00	14.00
2	110	45	110	95	115	120	120	125	125	100	116.00	97.00	19.00
3	85	55	80	50	75	50	80	60	90	70	82.00	57.00	25.00
4	130	95	135	105	140	100	130	125	130	130	133.00	111.00	22.00
5	100	100	120	100	125	110	125	125	130	115	120.00	110.00	10.00
6	130	135	135	135	130	130	130	130	135	135	132.00	133.00	1.00
7	130	95	125	145	125	125	120	120	120	95	124.00	116.00	8.00
8	90	30	90	40	85	75	100	55	90	90	91.00	58.00	33.00
9	100	55	104	88	120	100	120	120	120	120	112.80	96.60	16.20
10	105	50	125	115	130	100	130	55	130	95	124.00	83.00	41.00
Mean	110.50	75.00	114.90	99.80	117.50	105.00	119.50	102.50	121.00	107.50	116.68	97.96	18.92
Mean diff. with confidence limits[a]	35.50 ± 16.64		15.10 ± 13.90		12.50 ± 11.71		17.00 ± 18.64		13.50 ± 9.24		18.72 ± 8.54		

[a] $P > 0.05$ (except for the 4th injection)

and intravascular hemolysis and pulmonary hypertension associated with aortic coarctation has been described (8).

This study points out a need for continued investigation concerning the pharmacological actions of hemolyzed blood. Numerous observations remain unexplained and it would appear that there must be other factors, as yet undefined, which contribute to changes in the circulatory system.

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BOOK REVIEW

VETERINARY PHARMACOLOGY AND THERAPEUTICS, FOURTH EDITION. *Edited by L. Meyer Jones, Nicholas H. Booth and Leslie E. McDonald. Published by Iowa State University Press, Ames, Iowa. 1977. 1380 pages. Price $60.00.*

This book was prepared from the individual contributions of seventeen authors. It attempts to cover the whole field of veterinary pharmacology and drug usage and, in addition, contains a major section on veterinary toxicology. Two areas which do not apply to the Canadian situation are those on prescription writing and drug legislation and the area on drug and chemical residues in edible tissues. Much of what is written in these sections can be interpolated into the Canadian context. However, most of the specific examples used do not apply.

The section on drugs acting on the cardiovascular system and in particular the section on histamine, serotinin, etc. leaves much to be desired. A great deal of research effort has gone into this area in the last decade and a great deal of important new information has been obtained. This fact is not fully reflected in either the author's presentation or in his bibliographic section.

The autonomic and somatic nervous system is much improved over the fourth edition of Jones Veterinary Pharmacology and should suffice for the needs of the veterinary student and practitioner at the present time.

Drugs acting on the central nervous system, tranquilizers, etc. receive a great deal of attention in this textbook. The sections are well researched and well written. The major difficulty however is the fact that other textbooks devoted entirely to veterinary anaesthesia are currently available. These books have the advantage of more space, more illustrations and more practical information for the veterinary student or practitioner. Similar comments could be made regarding the toxicology section which is interesting reading and extremely well documented. Unfortunately it seems to be somewhat misplaced coming, as it were, at pages 1129 to 1288 of a 1380 page text. Indeed with some additional effort this section could be expanded to stand on its own, as a complete toxicology text.

In general the other sections of this book are well written and reflect a great deal of practical insight that will be useful to both the veterinary student and the private practitioner. Indeed the editors should take great satisfaction in the quality of this very large presentation. Unfortunately the cost is very high and will have a major limiting effect on its purchase by veterinary students. — *W. D. Black.*