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Intravenous Administration of Bovine Serum Albumin as a Blood Substitute in Experimental Secondary Shock.

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Recent workers[1] have advocated the intravenous administration of whole bovine plasma to human beings. In view of the high incidence of post-transfusion reactions reported by these workers,[1] it is surprising to note that no studies have been reported of the effect of bovine plasma in lower animals. The present paper constitutes preliminary observations upon the responses of dogs to the intravenous injection of bovine serum and plasma and of bovine serum albumin solution.

Material. Healthy dogs weighing from 2.9 to 8.8 kg were used throughout. Bovine serum and bovine plasma were separated from bovine blood by either the gravity or the centrifuge methods. The serum and plasma were then passed through a Seitz filter and stored in a refrigerator at 5°C. In several experiments the serum and plasma were diluted with an equal volume of isotonic saline solution (0.85% sodium chloride). In one experiment, bovine serum was mixed with an equal volume of canine blood. The resultant mixture of bovine and canine serums was separated from the blood cells by centrifugation and passed through a Seitz filter. Bovine serum albumin and bovine serum globulin were prepared by a method which will be described in a later communication together with blood chemical studies. In the present series of experiments the serum albumin obtained from several lots of bovine serum was pooled, and upon analysis revealed an albumin content of 6.7 g %. However, in the final experiment on Table I, the albumin content upon analysis was 4 g %. The bovine serum globulin was obtained from several lots of bovine serum and was pooled. Upon analysis, it revealed a globulin content of 6.4 g %. All the solutions were exposed to room temperature for several hours before being used.

Methods. Anesthesia was induced by nembutal in doses of 1/4 grain per kilo of body weight or by ether given by the open-drop method. The right carotid artery was cannulated and the arterial blood pressure recorded in the usual manner. The plasma, serum and

[1] Wangensteen, O. H., Hall, H., Kremen, A. J., and Stevens, B., PROC. SOC. EXP. BIOL. AND MED., 1940, **43**, 616.

serum albumin solutions were administered by gravity through a cannula inserted into the right femoral vein. Shock was produced by graded hemorrhage from the carotid artery. Blood was obtained when indicated from an ear of each animal and examined for evidences of agglutination of the red blood cells.

Results. The intravenous administration of whole bovine plasma or serum (150 cc to 400 cc) to normal dogs or to those suffering from hemorrhage resulted in the production of severe dyspnea, the respirations becoming stertorous and labored. The arterial blood pressure rose transiently and then fell gradually to zero. The blood of these animals showed no agglutination of the red blood cells. Dilution of the serum and plasma with equal amounts of isotonic sodium chloride solution did not prevent these toxic effects. Mixture of the serum with equal volumes of canine blood, and reinjection after separation of the blood cells were likewise ineffective. Postmortem examination of these dogs showed the presence of blood stained mucus in the bronchi and subpleural and subserosal petechiae. The spleen was moderately congested. The mucous membranes of the stomach and duodenum exhibited variable degrees of capillary congestion. The behavior of the animals and the absence of agglutination of the blood cells suggested that the fatal effects in these animals might be due to a foreign protein reaction. For this reason it was decided to study the effect of the intravenous administration of bovine serum globulin. This was given in amounts of 125 cc to 155 cc.

Dyspnea similar to that present in the animals which were given whole bovine serum or plasma occurred. The animals appeared to be very sick. The results of the intravenous administration of bovine serum albumin are illustrated in Table I. All of the animals recovered, and showed no obvious ill effects. The arterial blood pres-

TABLE I.
Effect of Intravenous Administration of Bovine Serum Albumin in Secondary Shock. Ether Anesthesia. All Recovered.

Dog wt. kg	Calc. blood vol., cc	Amt blood withdrawn, cc	Amt serum albumin sol. given, cc	Blood pressure		
				Initial, mm Hg	After bleeding, mm Hg	After injection, mm Hg
3.6	324	140	150	140	30	135
5.2	468	160	160	148	15	145
4.8	432	135	135	130	20	123
3.8	342	140	150	140	25	170
5.6	504	180	200	145	40	140
2.8	252	85	80	120	15	100
5.2	468	190	200	150	33	120

sure rose slowly during the injection to the initial level, while in a few animals it rose above the initial level. No disturbances of respiration, such as occurred in the other two groups of dogs, were noted.

Conclusions. Bovine serum, bovine plasma, and bovine serum globulin are very toxic when given by the intravenous route to dogs. The toxicity of the whole serum or plasma appears to be due to the serum globulin or related protein fractions. The intravenous administration of bovine serum albumin is not only harmless, but is effective in raising and maintaining the blood pressure of dogs subjected to severe hemorrhage. Since bovine blood is readily available, bovine serum albumin may prove useful as a substitute for blood. A study of the effects of the intravenous administration of bovine serum albumin in human beings will be reported later.

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Effect of Renal and Systemic Bloods from Normotensive and Renal Hypertensive Dogs on Arterial Rings.

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There are several reports claiming to have demonstrated the presence of a pressor substance in the systemic blood of renal hypertensive (Goldblatt) dogs[1, 2, 3] but other investigators have been unsuccessful in similar attempts.[4-9] Obviously this hypothetical pressor substance should be more easily detected in the venous return from the kidney of the renal hypertensive dog. Nevertheless, the reports

1 Govaerts, P., and Dicker, E., *Compt. rend. Soc. de biol.*, 1936, **122**, 809.

2 Solandt, D. Y., Nassim, R., and Cowan, C. R., *Lancet*, 1940, **1**, 873.

3 Page, I. H., *J. Exp. Med.*, 1940, **72**, 301.

4 Page, I. H., PROC. SOC. EXP. BIOL. AND MED., 1936, **35**, 112.

5 Collins, D. A., and Hoffbauer, F. W., PROC. SOC. EXP. BIOL. AND MED., 1937, **35**, 539.

6 Friedman, B., and Prinzmetal, M., *Ann. Int. Med.*, 1939, **12**, 1617.

7 Heymans, C., and Bouckaert, J. J., PROC. SOC. EXP. BIOL. AND MED., 1938, **39**, 94.

8 Katz, L. N., Friedman, M., Rodbard, S., and Weinstein, W., *Am. Ht. J.*, 1939, **17**, 334.

9 Wakerlin, G. E., and Yanowitz, M., PROC. SOC. EXP. BIOL. AND MED., 1939, **41**, 51.