

5. *Blackout.* The urines from 9 subjects[‡] who lost consciousness due to experimental acceleration (blackout rating of from 4.0 to 6.5 G) were examined. In no case was antidiuretic activity demonstrated in the urine.

6. *Electro-Convulsive Therapy.* Pooled urine samples were obtained from 3 separate groups of psychotic patients before and after E.C.T. The control specimens were devoid of activity, but following therapy marked antidiuretic activity was found.

7. *Eclampsia.* The urine of 7 cases of pre-eclampsia and of one eclamptic was examined and did not contain antidiuretic activity. The negative findings were not related to the associated albuminuria.

Discussion. The results which have been described show that an antidiuretic substance appears and may be extracted from the urine

[‡] These experiments were conducted through collaboration with Dr. W. R. Franks, R.C.A.F. Institute of Aviation Medicine, Toronto.

following certain procedures in man. The evidence, although indirect, indicates that this may be the posterior pituitary antidiuretic hormone. A more detailed discussion of these findings and the possible physiological mechanisms involved will be presented in a later paper(3).

Summary. An antidiuretic substance may be extracted from human urine following the intravenous injection of posterior lobe hormone, dehydration, fainting and electro-convulsive therapy.

The urine of normal persons, and subjects following loss of consciousness associated with "blackout" does not contain antidiuretic activity under the experimental conditions described. The urine of eclamptic women was also inactive.

3. Noble, R. L., Plunkett, E. R., and Taylor, N. B. G., *Rec. Advances Hormone Res.*, Vol. IV, Academic Press, N.Y., 1949.

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Production of a Hemorrhagic State by the Infusion of Hemolyzed Blood.* (17629)

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While conducting experiments relative to the development of a mechanical pump-oxygenator for the temporary deviation of blood from the heart and lungs of dogs, hemolysis was frequently encountered. At this time, dogs died of a previously undescribed hemorrhagic state which closely simulated a condition seen on occasion in man. It was therefore deemed advisable to devise a more simple method of reproducing this condition. Since that time, changes in pump-oxygenator have been effective in eliminating hemolysis, and

the incidence of this syndrome has been diminished.

This entity is characterized by prolonged or infinite blood coagulation time, and poor clot retraction. This blood will clot *in vitro* by the addition of small amounts of thromboplastin or fresh blood from another dog. This reversal is only temporary *in vivo*, however. Hemorrhage occurs from the entire gut which is contracted, pitted, granular and is studded throughout with petechiae. Bloody effusions invade the serous cavities. Petechiae also appear in the lungs, serosal surfaces and along blood vessels. Microscopically the liver and spleen show parenchymal congestion with erythrocytes and pigment and the kidney tubules and glomeruli also contain pigment. Portions of this syndrome

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TABLE I.
Infusion of Heparinized Whole Blood, 3 Hours to 3 Days Old.

Dog	Vol. blood exchanged cc/kg	Method of hemolysis	Amt hemoglobin infused, g/kg body wt	Syndrome	Coagulation time			
					Max.	Hr after infusion	Subsequent min.	Hr after infusion
1	70	Hemolyzing pump	4.1	+	∞	$\frac{1}{4}$	∞	*
2	105	"	3.3	+	22'	1	19'	$\frac{1}{2}$
3	118	Shaking	2.2	+	∞	$\frac{3}{4}$	∞	
4	123	Not hemolyzed	0.2	—	16'	$\frac{1}{2}$	5'	2

* Coagulation time temporarily reduced to three min. by thromboplastin intravenously.

TABLE II.
Infusion of Citrated Blood, Twenty-six to Thirty-four Days Old.

Dog	Vol. infused cc/kg	Method of hemolysis	Components present		Amt plasma Hbg. infused g/kg	Syndrome	Max. coagulation time
			Hemoglobin	Stroma			
5	32	Shaking	+	+	1.44	+	2½ hrs
6	36	Distilled water	+	0	2.9	+*	2½ hrs
7	44	Not hemolyzed			0.012	—	4 min.
8	21	Stroma in saline (no blood)	0	+	0.0	—†	4 min.

* No serosal or perivascular petechiae.

† Petechiae but no hemorrhage or increase in coagulation time.

have been observed as Barratt and Yorke(1) found that larger doses of hemolyzed blood were tolerated and sudden death avoided if stroma was removed from hemolyzed blood. They also noted aberrations in clotting time. Flink(2) observed in one dog the same gross pathology that we report but made no observations on coagulation time.

Methods. All dogs were anesthetized with pentobarbital sodium or pentothal and cross matched. Donor blood was drawn from normal animals using 30 mg heparin or 240 cc A.C.D.† solution per liter for anticoagulant as indicated. Hemolysis was produced in one of 3 ways: (1) blood was run for 20 minutes through a pump known to produce hemolysis, (2) blood was shaken manually until plasma hemoglobin reached desired level, (3) refrigerated citrated blood was treated by decanting the plasma and washing the red blood cells 3 times with isotonic saline. One hundred cc distilled water were added to 200 cc red

blood cells with centrifugation for one hour at approximately 2000 r.p.m. to separate the stroma from the supernatant fluid. In Experiment I, arterial blood was withdrawn in volume equal to that of the intravenous infusion. Coagulation times were determined by a modified Lee-White method; plasma hemoglobins were done by the acid hematin and oxyhemoglobin methods.

Results are shown in Tables I and II.

Discussion. Hemolysis does not appear to be the only factor in operation, as this syndrome has been observed in dogs with a lower plasma hemoglobin than that in certain other surviving animals. Plasma hemoglobin alone is apparently not the sole cause as I.V. administration of distilled water sufficient to raise plasma hemoglobin above 1.0 gram per cent will not cause this condition. Studies to elucidate etiological factors are being pursued in our laboratory at the present time.

Summary. A syndrome of prolongation of blood coagulation time, gastro-intestinal bleeding and petechiae is described. This condition can be produced in the dog by the infusion of hemolyzed blood.

1. Barratt, J. O. W., and Yorke, W., *Brit. M. J.*, 1914, v1, 235.

2. Flink, E. B., *J. Lab. and Clin. Med.*, 1947, v32, 223.

† A.C.D. solution contains 2.45% dextrose, 1.37% sodium citrate, 0.50% citric acid in distilled water.