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A Hemophilia-Like Disease in Swine.*

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During the last few years a number of swine in the Missouri Agricultural Experiment Station† herd have died from hemorrhage, either spontaneous or as a result of minor wounds. All of the affected animals are closely related. It is evident that the blood-clotting mechanism is seriously defective, and a study was initiated in an attempt to classify the abnormality.

Bleeding Time. If determined by Duke's method[1] the bleeding time is within the normal range. As shown in Table I though, if an incision of any extent is made the bleeding time is prolonged indefinitely.

Coagulation Time. The procedure followed is essentially the same as the Lee-White[2] modification of Howell's method. The blood sample is taken from an ear vein, collected in cold paraffin coated tubes, and placed in an ice bath. The results reported in Table I show that the coagulation time was 5 times that of normal blood. The blood clots slowly, but after it forms it retracts in normal time.

According to the prevailing theory at least 4 components of the blood are intimately concerned with blood coagulation: (1) calcium; (2) prothrombin; (3) fibrinogen; (4) thromboplastin, which presumably is released from the platelets and other formed elements. Each one has been subjected to preliminary investigation.

TABLE I.
Bleeding Time, and Coagulation Time of Blood.

Observation	Type of animal	
	Normal	Defective
Bleeding time, sec.		
1 cm stab in ear with 18-gauge needle	140	155
1 cm slit in edge of ear	215	bled to death
Coagulation time, min.	28	145

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1 Duke, W. W., *J. A. M. A.*, 1910, **55**, 1185.

2 Lee, R. I., and White, P. D., *Am. J. M. Sci.*, 1913, **145**, 495.

Calcium Time. According to our observations the calcium time[3] is not less than the coagulation time, and the serum calcium was shown by analysis to be well within the normal range. Our data on calcium are omitted from the tabulations.

Fibrinogen Content. Oxalated plasma was diluted with isotonic saline and recalcified. The resulting fibrin was removed and determined quantitatively. The data shown in Table II indicate that the blood of defective animals contains slightly less fibrinogen than does that of normal controls, but the quantity is more than enough to form a normal clot.

Prothrombin Time and Thromboplastin. The prothrombin time was determined both by the method of Howell[4] and of Smith, *et al.*[5] The prolonged prothrombin time obtained by Howell's method could be due to an abnormally low level of either prothrombin or thromboplastin. Since the prothrombin time by Smith's method is normal, it is concluded that the blood of the defective animals is deficient in available thromboplastin. The data are summarized in Table II.

TABLE II.
Quantitative Determinations Related to the Coagulation Time of Blood.

Type of animal	Prothrombin time		Fibrinogen in plasma %	Platelets	
	Howell min	Smith sec		No. per mm³ × 1000	Vol. %
Normal	15	30	.54	205.0	.42
Defective	110	30	.45	179.7	.59

Blood Platelets. The platelet counts were made by the indirect method, essentially as described by Gradwohl[6] and by the direct method of Rees and Ecker.[7] Platelet volume was also determined by the method of Van Allen.[8] The data in Table II indicate that the platelet count in defective swine is not significantly different from that in normal animals. However, the volume of platelets is higher in the blood of defective animals, presumably because they are more stable. Platelet counts were made on blood that had stood for

[3] Todd, J. C., and Sanford, A. H., *Clinical Diagnosis by Laboratory Methods,* 8th Ed., Saunders, Philadelphia, 1936, p. 217.

[4] Howell, W. H., *Arch. Int. Med.,* 1914, **13**, 76.

[5] Smith, H. P., Ziffren, S. E., Owen, C. A., and Hoffman, G. R., *J. A. M. A.,* 1939, **113**, 380.

[6] Gradwohl, R. B. H., *Clinical Laboratory Methods and Diagnosis,* Mosby, St. Louis, 1935, p. 258.

[7] Rees, H. M., and Ecker, E. E., *J. A. M. A.,* 1923, **80**, 621.

[8] Van Allen, C. M., *J. Lab. Clin. Med.,* 1926, **12**, 282.

varying periods of time, following the procedure of Howell and Cekada.[9] The blood was collected in paraffin-coated tubes which were kept cool in an ice bath. At regular intervals of time blood smears were made on a glass slide, dried, and stained by Wright's method.[10] The specimens were examined for the relative number of platelets and for the degree of agglutination that had occurred. The data presented in Table III show that the platelets disintegrate more rapidly in normal than in abnormal blood. These studies indicate that the platelets from defective animals are abnormally stable, and at present this is the most obvious explanation of the abnormalities observed.

The symptoms resemble hemophilia more closely than they do any other disease that has come to our attention.

TABLE III.
Stability of Platelets.

Type of animal*	Min. after collection	No. platelets per 1000 erythrocytes	Remarks
Normal	5	39	A considerable number adhering in pairs
Defective	5	32	No agglutination
Normal	30	17	Agglutinated and ragged
Defective	30	27	No agglutination

*The data are averages of 2 normal and of 2 defective animals.

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Return of Hepatic Vitamin A in Rats after Depletion by Methylcholanthrene.

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Goerner[1] demonstrated that a gelatin suspension of 1,2,5,6-dibenzanthracene injected intraperitoneally into rabbits markedly decreased the vitamin A content of the liver mitochondria. In surviving animals the vitamin content of these structures was slowly restored after the drug was discontinued. Later Goerner and

[9] Howell, W. H., and Cekada, E. B., *Am. J. Physiol.*, 1926, **78**, 500.

[10] Wright, J. H., *J. A. M. A.*, 1910, **55**, 1979.

[1] Goerner, A., *J. Biol. Chem.*, 1937, **122**, 529.