

3. Closed aseptic intestinal loops in which the blood supply is completely shut off are not incompatible with life.

4. Bacterial activity plus the necrotic tissue or the results of the action of bacteria on necrotic tissue is the important factor in the rapid death in simple closed intestinal loops.

5. The normal secretions of the duodenum and jejunum are not toxic when allowed to drain into the abdominal cavity.

6. Our results do not support the theory of Draper of a normal toxic secretion of the duodenal mucosa, neutralized by the jejunal mucosa, or the perverted secretion theory of Whipple.

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### **The effect of intravenous injections of fresh human serum and of phosphated blood, on the coagulation time of the blood in hereditary hemophila.**

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The coagulation time of the blood in hereditary hemophilia fluctuates in an irregular manner from day to day. Only very pronounced alterations are therefore of value as a guide to the effect of any particular method of treatment. The variations shown in Table I were observed in cases who were not subjected to any treatment. In many instances the changes observed are well beyond the error of the method which was used. Five cubic centimeters of blood were withdrawn from the median basilic vein through a short oiled needle into two or more test-tubes, and the average interval of time required until coagulation had advanced sufficiently to allow of the complete inversion of the tubes without spilling the contents was taken as the coagulation time. The temperature was 37° C. Normal blood requires about 13 minutes to coagulate under these conditions. Parallel observations with another method showed that reliable results could be obtained with blood from skin puncture when certain details in the manner of collecting the blood were observed.<sup>1</sup>

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<sup>1</sup> Addis, T., *Edin. Med. Journ.*, 1910, V, 38.

TABLE I.

VARIATIONS IN THE COAGULATION TIME OF HEMOPHILIC BLOOD OCCURRING IN CASES NOT SUBJECTED TO ANY TREATMENT.

Case I.		Case II.		Case III.	
Date.	Coag. Time. Minutes.	Date.	Coag. Time. Minutes.	Date.	Coag. Time Minutes.
Aug. 21	60	Sept. 19	60	Sept. 15	38
" 22	53	" 22	87	" 18	54
" 23	50	" 23	70	" 20	80
" 24	67			" 23	52
" 25	66				
" 26	68				
" 30	88				
" 31	96				
Sept. 4	67				
" 5	81				
" 10	55				
" 11	71				
" 19	65				
" 23	76				

Variations in coagulation time which were not greater than those illustrated in Table I were noted under the administration by mouth of calcium lactate, sodium chloride and of large quantities of raw beef juice. The removal from a vein of 60-70 c.c. of blood once a week had no effect.

No immediate effect was produced by the intravenous injection of normal horse serum and of antidiphtheritic serum. These sera were all five or more weeks old. In one case a marked prolongation of coagulation time was found three weeks after an intravenous injection of horse serum, but since successive observations were not made during this interval, it is not certain that this was the result of the serum injection.

The intravenous injection of 15 c.c. of human serum separated from freshly drawn blood ninety-six hours previously was followed within 15 minutes by a striking decrease in the coagulation time. There was a gradual increase in the coagulation time during the next week and on the tenth and twelfth days after the injection, the coagulation time was considerably longer than before the serum was given. Three weeks later the coagulation time was again at its usual level. The details of this experiment are given in Table II. The method of skin puncture was used.<sup>1</sup> Each figure is the average of six estimations.

TABLE II.

VARIATION IN THE COAGULATION TIME OF CASE I FOLLOWING THE INTRAVENOUS INJECTION OF HUMAN SERUM, NINETY-SIX HOURS OLD.

Date.		Coagulation Time. Minutes.	Remarks.
Feb. 24		72	Normal coagulation time 10 min.
Feb. 26		89	
Feb. 28		72	
Mar. 2	3 P.M.	62	15 c.c. human serum 96 hours old injected intravenously.
	4 P.M.		
	4:15 P.M.	24	
	6:00 P.M.	27	
	8:00 P.M.	33	
Mar. 5	2:00 A.M.	34	
	12 Noon	39	
Mar 6		40	
" 7		49	
" 10		59	
" 12		77	
" 14		127	
" 16		114	
" 17		103	
" 20		94	
" 22		86	
" 24		83	

The intravenous injection of freshly drawn whole blood to which sodium phosphate had been added as an anti-coagulant,<sup>1</sup> had the immediate effect of making the coagulation time ten times shorter. But here again as after the injection of fresh serum, this decrease was succeeded by a gradual lengthening of the time. Unfortunately it was not possible to continue the observations beyond the eighth day, so that it is not known whether there was a later increase in the coagulation time beyond the time required before the injection. These results were obtained with the method of venous puncture. They are given in Table III, which also shows another experiment, illustrating the immediate reduction in coagulation time caused by fresh human serum.

The recalcified oxalated plasmata prepared from blood drawn from Case 1 and Case 2 after the injection of fresh human serum coagulated in a considerably shorter time than the recalcified plasmata prepared from blood drawn before the injection. The rate of formation of thrombin was more rapid after serum injection

<sup>1</sup> One part of 5 per cent. sodium phosphate to three parts of blood.

TABLE III.

VARIATION IN THE COAGULATION TIME OF CASE I FOLLOWING THE INTRAVENOUS INJECTION OF ABOUT 300 C.C. OF FRESHLY DRAWN HUMAN PHOSPHATED BLOOD.

Date.		Coagulation Time, Minutes.	Remarks.
May 16		245	Normal coagulation time—13 min.
" 20	11 A.M.		About 300 c.c. of human phosphated blood injected intravenously.
	12 Noon.	24	
" 22		30	
" 24		32	
" 28		55	
June 14	10 A.M.	200	
	10:15 A.M.		8 c.c. of human serum 20 hours old injected intravenously.
	12 Noon.	38	

than before. Smaller amounts of normal plasma were required to reduce the coagulation time of the recalcified plasma to normal after serum injections than before. It was concluded that the serum injection had altered the pro-thrombin content of the blood.

These observations were made in 1910 in the Laboratory of the Royal College of Physicians in Edinburgh during the tenure of a Carnegie Research Fellowship. It was hoped that they might be completed and extended before publication, but this has not been possible. They are of interest in connection with a recent report by Ottenberg<sup>1</sup> on the effect of citrated blood and of citrate solution on the coagulation time in hereditary hemophilia.

#### CONCLUSIONS.

1. The intravenous injection of fresh human serum causes an immediate shortening of the coagulation time of the blood in cases of hereditary hemophilia. There is then a gradual lengthening of the time until it is considerably longer than before the injection, and finally a return to the original level.

2. The intravenous injection of fresh whole blood prevented from coagulating by the addition of sodium phosphate caused a similar immediate decrease, and was followed by a gradual increase in the coagulation time during the subsequent eight days.

3. An alteration of the pro-thrombin content of the plasma-

<sup>1</sup> Ottenberg, R., *PROC. SOC. EXP. BIOL. AND MED.*, 1916, 13, 104.

was found to be the cause of the increased coagulability of the blood after intravenous injections of fresh normal serum.

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**Notes on the occurrence of equine sporotrichosis in Montana and the "blastomycotic" form of *Sporotrichum schencki-beurmanni*.**

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In 1915 I<sup>1</sup> expressed the belief, based on very inadequate material, that animal sporotrichosis is found also in Montana. Quite recently, through the courtesy of Doctor DuFrene, of Glendive, fresh pus collected from a case of equine sporotrichosis was forwarded to me for diagnosis. Without the least difficulty a typical *Sporothrix schencki-beurmanni* was isolated on Sabouraud medium, and conclusive bacteriologic evidence was thereby obtained that sporotrichosis exists endemically in Montana.

As is customary in our studies on fungi, plain one per cent. glucose agar was inoculated with the pus. The growth on this medium remained perfectly white and thin, becoming thick, moist, very stringy and inelastic in contrast to the typical well-pigmented folded film observed on Sabouraud's agar. The culture did not penetrate into the superficial layers of the agar, and was easily emulsified. It grew well under anaerobic conditions, and produced a rapid septicaemia in rats and rabbits. On one per cent. glucose agar and plain potato, this pleomorphism has remained so far (three weeks and four transplants) constant, but on Sabouraud medium the typical growth invariably appeared in a short time.

Microscopically, such a culture consists of oblong, oval or round, short, monilia-like mycelia with a well-marked double membrane and refractile granules. Some round forms show reproduction by budding and aggregations in pairs or short chains. Long mycelia with typical clusters of spores were always absent.

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<sup>1</sup> *Jour. A. M. A.*, 1915, LXV, p. 519.