STUDIES ON CEANOTHYN AS A BLOOD COAGULANT IN MAN.*

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Introduction.—A preliminary report of this work was published by the Council on Pharmacy and Chemistry (1) of the American Medical Association. The purpose of this paper is to give a detailed account of the investigation into the effectiveness of the oral administration of Ceanothyn as a coagulation-time depressant of human blood.

Material and Methods.—An account of the preparations used is given in the above report. Briefly, they were these: (1) coagulant Mixture A., which contained "fluidextract of wild cherry, 10 cc.; tincture of caramel, 10 cc.; spirit of cinnamon, 0.15 cc.; syrup enough to make 450 cc." (2) coagulant Mixture B., and (3) coagulant Mixture C. Mixtures B. and C. contained Ceanothyn. Until the preliminary report had been submitted, we were not informed as to the contents of the mixtures.

The subjects used in this study were divided into four groups: (1) received nothing; (2) received coagulant Mixture A.; (3) received coagulant Mixture B.; (4) received coagulant Mixture C. The subjects of the groups were members of the laboratory staff and patients on the wards of the Third (New York University) Medical Division, Bellevue Hospital.

The diagnoses of the patients were as follows: chronic lymphatic leukemia; alcoholic polyneuritis; *diabetes mellitus;* acute catarrhal jaundice; pernicious anemia; chronic myelogenous leukemia; duodenal ulcer; Banti's disease; *dermatitis exfoliativum;* rheumatoid arthritis; ulcerative colitis, non-specific; tabes dorsalis; acute epidemic cerebrospinal meningitis; rheumatic heart disease, active; carcinoma of liver; Hodgkin's disease; Henoch-Schönlein's purpura; acute lymphatic leukemia; thrombocytopenic (idiopathic) purpura; luetic anemia; polycythemia vera; lymphosarcomatosis; chronic ulcerative pulmonary tuberculosis; acute rheumatic polyarthritis.

The methods used for determining the coagulation time were (1) the capillary glass-tubing method; (2) the method of Lee and White. Conditions were standardized in that the same end-points were used throughout, the temperature was maintained constant and the same observer made all the readings of a single test. Taylor (2) used the capillary tube method described by Payne in most of his human subjects and an adaptation of the method of Howell in a series of rabbits for comparison. According to the method used, the subjects were grouped as follows: capillary glass-tubing method—40 subjects, 39 of whom had simultaneous, duplicate determinations, giving a total of 79 complete sets of determinations; method of Lee and White—16 subjects, all of whom had simultaneous, duplicate determinations, giving a total of 32 complete sets of determinations.

The coagulant mixtures were given, undiluted, and by mouth after making control, simultaneous, duplicate determinations. The details of dosage and of time of administration are given in the tables.

Results and Conclusions.—Vomiting occurred three times: cases 19, 27 and 47, after the patients had received 30, 60 and 90 cc., respectively, of the coagulant

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mixtures. (See tables.) Excepting the vomiting and rarely a feeling of nausea, no toxic symptoms were noted even when doses of 120 cc. were used.

The results are given in Tables I, II, III and IV. From a study of these data it is quite obvious that the results of the coagulation time determinations in those patients who received no coagulant mixture and those who received coagulant Mixture A. (no Ceanothyn) and the patients who received Ceanothyn (coagulant Mixtures B. and C.) are quite comparable.

From these results we can adduce no proof that the oral administration of Ceanothyn decreases the clotting time of blood in man.

TABLE I.

Coagulant Mixture A.		Coagulation Time in Minutes and Seconds (Capillary Tube Method).							
Case number.	Determination.	Time Elapsed after Control Determination. Control.	15 min.	30 min.	45 min.	60 min.	75 min.	90 min.	105 min.
1	I	5′10″*	5′00″	6′00″	6′05″	5′00″			
2	I	8′10″*	7′10″	6′25″	2′50″	1′50″			
	II	8′15″	4′50″	4′40″	3′30″	2′10″			
3	I	3′40″*	4′00″	2′45″	3′00″*	4′00″	2′30″	2′45″	
	II	2′30″	3′20″	3′45″	3′30″	3′30″	2′10″	3′15″	
4	I	3′45″†	2′30″	3′00″	2′35″	2′40″	3′10″		
	II	5′00″	2′45″	2′30″	2′15″	2′20″	2′20″		
5	I	5′00″†	3′00″	4′30″	4′00″	4′45″	4′00″		
	II	5′00″	3′15″	4′30″	3′40″	4′30″	3′30″		
6	I	3′00″†	3′05″	3′10″	3′05″	3′10″			
	II	2′40″	2′45″	2′30″	2′45″	2′40″			
7	I	5′20″†	4′20″	5′20″	4′20″†	2′10″	3′10″	3′20″	
	II	5′00″	3′30″	5′10″	3′20″	2′20″	2′50″	2′50″	
8	I	4′40″†	3′35″	4′15″	3′40″†	3′50″	3′50″	4′25″	
	II	3′40″	3′15″	3′55″	3′10″	2′50″	3′10″	4′15″	
9	I	4′00″*	3′50″	6′00″	2′30″*	4′15″*		4′00″*	4′00″
	II	4′20″	3′20″	6′30″	3′00″	4′30″		3′45″	4′50″
10	I	4′50″†	3′45″	5′20″	3′40″	4′10″	3′30″	3′15″	
	II	3′50″	4′45″	4′00″	2′30″	3′30″	3′00″	2′35″	
11	I	5′35″*	5′50″	5′50″*	5′30″	4′25″*	6′10″	4′35″*	5′20″
	II	6′15″	4′50″	5′20″	5′30″	3′55″	5′30″	3′35″	4′00″
12	I	2′30″*	3′45″	3′00″*	4′15″	2′25″*	3′35″	2′50″*	2′40″
	II	2′05″	3′25″	2′00″	3′25″	2′05″	2′55″	2′00″	2′10″
13	I	4′40″*	4′40″	3′20″*	4′10″	3′54″*	3′00″	3′40″*	3′25″
	II	4′10″	5′00″	2′40″	3′30″	3′40″	2′10″	3′10″	3′05″
				No Mixture.					
14	I	4′25″	4′10″	3′55″	2′30″	2′55″	2′45″	4′20″	2′50″
	II	3′55″	3′10″	3′15″	2′10″	2′35″	3′05″	4′00″	2′40″
15	I	4′14″	4′15″	4′25″	4′45″	4′20″	4′00″	4′35″	4′35″
	II	3′20″	3′55″	3′55″	4′25″	3′30″	3′30″	4′05″	3′55″
16	I	4′55″	4′30″	4′50″	3′50″	4′10″	3′50″	4′00″	4′05″
	II	3′45″	3′20″	2′50″	2′30″	3′50″	2′30″	3′20″	2′55″
17	I	5′30″	4′25″	4′20″	4′00″	4′40″	4′14″	3′55″	2′50″
	II	4′00″	3′25″	2′50″	3′00″	3′20″	2′40″	3′05″	2′20″
18	I	6′20″	4′30″	4′50″	4′05″	4′45″	4′45″	3′50″	4′20″
	II	5′20″	3′20″	4′20″	3′25″	3′45″	3′05″	3′10″	3′30″

I and II are determinations done as nearly simultaneously as was possible from a single skin puncture. * and † signify the administration of 15 and 30 cc., respectively, of a coagulant mixture. The mixture was given immediately after taking the samples of blood.

TABLE II.

Coagulant Mixture B. Coagulation Time in Minutes and Seconds (Capillary Tube Method).

Case number.	Determination.	Time Elapsed after Control Determination. Control.	15 min.	30 min.	45 min.	60 min.	75 min.	90 min.	105 min.
19	I	3′00″*	3′30″	3′00″*	3′15″	*	3′10″	*	3′40″
	II	2′40″	3′00″	2′30″	3′00″		3′30″		3′30″
20	I	5′15″*	4′00″	3′25″*	2′30″	2′25″*	2′00″	2′20″*	2′00″
	II	4′15″	3′40″	3′15″	2′45″	2′45″	2′10″	2′00″	1′00″
21	I	3′45″*	3′20″	4′20″*	3′20″	4′40″*	3′00″	*	4′10″
	II	3′25″	2′40″	3′20″	3′10″	4′30″	2′50″		3′30″
22	I	3′40″*	3′40″	3′40″*	4′20″	4′15″*	3′50″	4′30″*	4′00″
	II	2′50″	4′10″	3′20″	4′30″	3′55″	3′40″	3′40″	4′16″
23	I	3′20″*	3′10″	4′10″*	3′05″	4′05″*	4′55″	3′40″*	3′10″
	II	3′00″	3′00″	4′00″	2′45″	3′25″	3′55″	3′20″	3′20″
24	I	6′15″*	5′20″	6′10″*	3′05″	4′25″*	4′15″	4′20″*	3′55″
	II	5′15″	4′40″	5′10″	3′15″	5′25″	2′35″	3′10″	2′45″
25	I	6′30″*	6′10″	6′35″*	6′50″	6′10″*	5′30″	7′15″*	9′10″
	II	5′30″	4′50″	5′15″	5′40″	5′50″	6′00″	6′30″	8′50″
26	I	3′10″*	2′30″	2′40″*	3′15″	2′46″*	3′30″	2′40″*	3′20″
	II	2′00″	2′10″	2′20″	2′45″	2′10″	2′50″	2′10″	3′10″
27	I	4′50″*	3′10″	2′25″*	2′30″	4′40″*	3′20″	3′10″*	3′10″
	II	4′20″	3′20″	2′15″	2′10″	3′50″	3′00″	2′50″	4′10″
28	I	4′00″*	3′00″	4′20″*	3′10″	3′46″*	3′40″	3′55″*	4′25″
	II	3′40″	2′20″	3′50″	2′50″	3′30″	3′00″	3′35″	2′45″
29	I	3′45″*	3′40″	4′05″*	4′24″	3′40″*	3′50″	3′10″*	3′00″
	II	3′25″	3′54″	3′55″	4′00″	2′30″	2′50″	2′00″	2′00″
30	I	5′15″*	3′15″	3′40″*	4′30″	3′55″*	4′50″	3′55″*	3′15″
	II	4′55″	3′00″	3′00″	4′10″	3′15″	4′00″	3′05″	3′05″

I and II are determinations done as nearly simultaneously as was possible from a single skin puncture. * and † signify the administration of 15 and 30 cc., respectively, of a coagulant mixture. The mixture was given immediately after taking the samples of blood.

TABLE III.

Coagulant Mixture C. Coagulation Time in Minutes and Seconds (Capillary Tube Method).

Case number.	Determination.	Time Elapsed after Control Determination. Control.	15 min.	30 min.	45 min.	60 min.	75 min.	90 min.	105 min.
31	I	4′20″*	5′35″	4′25″*	4′30″	3′53″*	3′50″	4′35″*	5′25″
	II	4′00″	4′35″	3′55″	4′00″	3′15″	3′10″	5′45″	4′25″
32	I	4′20″*	4′10″	3′50″*	4′00″	4′00″*	3′50″	3′50″*	3′40″
	II	3′50″	4′00″	3′30″	4′20″	3′40″	4′10″	4′10″	3′30″
33	I	7′30″*	6′35″	4′00″*	5′40″	3′10″*	6′50″	4′45″*	5′25″
	II	5′00″	4′35″	3′40″	5′10″	2′50″	6′30″	3′45″	4′05″
34	I	4′20″*	3′35″	3′50″*	3′35″	3′40″*	5′00″	4′30″*	4′00″
	II	3′50″	3′55″	3′30″	2′25″	3′30″	4′00″	3′50″	4′20″
35	I	3′15″*	2′50″	4′50″*	3′10″	3′45″*	2′25″	2′45″*	3′25″
	II	3′05″	2′40″	4′30″	3′00″	3′25″	2′15″	3′05″	3′15″
36	I	5′55″*	5′30″	6′40″*	6′50″	6′20″*	6′25″	6′00″*	7′10″
	II	4′15″	4′10″	5′50″	6′20″	5′50″	5′55″	5′30″	6′50″
37	I	3′30″*	4′05″	4′05″*	4′05″	4′55″*	3′40″	4′05″*	4′10″
	II	3′40″	3′05″	4′15″	3′05″	4′35″	3′30″	3′35″	3′10″
38	I	6′50″*	5′10″	5′40″*	6′20″	6′05″*	5′10″	6′50″*	4′50″
	II	8′20″	5′30″	5′10″	6′40″	6′25″	4′20″	7′20″	4′00″
39	I	4′30″*	4′10″	4′15″*	3′50″	4′55″*	5′15″	4′15″*	4′00″
	II	3′30″	3′50″	4′05″	3′40″	4′45″	3′45″	3′30″	3′30″
40	I	4′00″*	3′50″	3′20″*	4′40″	4′05″*	3′50″	3′50″*	3′20″
	II	3′00″	2′50″	2′50″	3′10″	2′55″	2′50″	2′30″	2′30″

I and II are determinations done as nearly simultaneously as was possible from a single skin puncture. * and † signify the administration of 15 and 30 cc., respectively, of a coagulant mixture. The mixture was given immediately after taking the samples of blood.

TABLE IV.

No Mixture. Case number.	Determination.	Coagulation Time in Minutes and Seconds (Lee and White Method). Time Elapsed after Control Determination. Control.	15 min.	30 min.	45 min.	60 min.	75 min.	90 min.	105 min.
41	I	7′00″	9′00″	7′30″	5′00″	2′45″	5′35″	10′00″	
	II	5′00″	11′00″	5′30″	5′00″	2′55″	4′30″	12′00″	
42	I	7′00″	6′00″	8′00″	6′30″	12′35″	10′30″	14′00″	
	II	7′10″	10′00″	8′15″	7′00″	6′40″	11′00″	11′00″	
43	I	9′00″	9′00″	9′30″	16′10″	12′15″	9′30″	11′45″	
	II	7′10″	13′10″	16′45″	13′15″	8′00″	6′10″	5′15″	
44	I	8′00″	6′00″	5′00″	6′50″	9′30″	8′50″	5′00″	
	II	10′00″	8′00″	5′10″	6′00″	9′10″	8′40″		
45	I	5′00″	11′20″	10′30″	7′50″	7′20″	4′50″	5′30″	6′30″
	II	10′50″	6′10″	8′30″	6′10″	8′00″	5′00″	9′30″	10′45″
46	I	9′00″	8′15″	8′15″	10′10″	9′15″	10′00″	11′50″	
	II	8′30″	7′15″	7′15″	9′00″	8′25″	5′00″	9′10″	
		Coagulant Mixture A.							
47	I	10′ †	5′00″	14′30″†	11′30″	13′00″†	11′20″	7′00″†	8′00″
	II	12′00″	10′30″	11′00″	18′00″	16′30″	9′40″	10′00″	12′00″
48	I	5′00″†	7′00″	5′00″†	4′00″	4′00″†	3′30″		
	II	5′10″	9′00″	5′10″	4′30″	4′20″	4′00″		
49	I	15′00″†	5′30″	6′00″†	5′00″	5′00″†	7′00″		
	II	12′10″	10′50″	6′20″	8′10″	5′00″	8′30″		
50	I	9′00″†	10′30″	6′00″	7′00″	11′00″			
	II	8′30″	7′45″	7′30″	13′30″	6′30″			
		Coagulant Mixture B.							
51	I	18′00″†	11′00″	†	9′30″	10′00″†	7′00″	14′00″	
	II	19′30″	12′30″		8′30″	7′30″	11′00″	12′00″	
52	I	13′00″†	8′40″	10′00″†	9′00″	7′20″†	3′00″	5′00″†	9′00″
	II	13′00″		11′00″	11′00″	9′00″		2′20″	9′00″
53	I	5′30″†	5′30″	10′00″†	6′20″	5′00″	9′30″		
	II	7′00″	4′00″	6′30″	6′20″	5′10″	8′20″		
		Coagulant Mixture C.							
54	I	6′10″†	5′30″	4′00″†	3′35″	4′00″†	2′00″		
	II	6′20″	5′10″	4′50″	4′20″	4′00″	2′00″		
55	I	6′00″†	7′00″	12′30″†	7′00″	5′00″†	5′10″		
	II	8′00″	6′00″	5′00″	7′00″	5′10″	7′00″		
56	I	8′00″†	6′00″	10′00″†	12′00″	8′00″†	8′10″		
	II	8′00″	6′00″	10′00″	10′00″	8′00″	8′20″		

I and II are determinations done as nearly simultaneously as was possible from a single venar puncture. † signifies the administration of 30 cc. of a coagulant mixture. The mixture was given immediately after taking the samples of blood.

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