

Effect of Oxalic Acid Given Intravenously on the Coagulation Time in Hemophilia.

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Steinberg and Brown¹ reported the preparation of extracts from certain plants which they stated, caused a rapid acceleration of the rate of coagulation of blood. The active agent in this extract was identified as oxalic acid. They stated that elevation in the clotting time was attended by a fall in blood oxalic acid, while reduction in clotting time conversely resulted in a rise in the oxalic acid content of the blood. The extract was marketed under the name Koagamin.

Steinberg² indicated that this extract was effective in hemophilia. Schumann,³ reporting on the use of Koagamin in the control of hemorrhage, stated that Koagamin had been used in hemophilia with gratifying results. However, he gives no data nor references to illustrate that fact. Page and coworkers⁴ recently reported 3 hemophiliacs in whom the coagulation time was said to become normal after the injection of oxalic acid intravenously. They stated that one of the cases became refractory to oxalic acid injections after the first course of therapy. They used 3 to 5 cc of a 0.1% solution of oxalic acid 3 times daily. These results, if confirmed, would represent a tremendous advance in the clinical management of hemophilia.

This communication reports the use of oxalic acid in 5 cases of hemophilia. Two of the cases were also treated with Koagamin. Our results indicate that neither Koagamin nor oxalic acid causes any reduction in the coagulation time in hemophilia.

Method of Study. Five hemophiliacs from 4 different families were used in the study. These patients all have typical family histories and clinical findings of the disease. The coagulation time was measured by the following procedure: The coagulation tubes were 8 mm in diameter. They had been cleaned with bichromate-

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¹ Steinberg, Arthur, and Brown, William R., *Am. J. Physiol.*, 1939, **126**, 638.

² Personal communication.

³ Shumann, Edward A., *Am. J. Ob. and Gyn.*, 1939, **38**, 1002.

⁴ Page, R. C., Russell, H. K., and Rosenthal, R. L., *Ann. Int. Med.*, 1940, **14**, 78.

sulphuric acid solution, rinsed with distilled water and, just before using, were again rinsed with physiological saline. Twenty-five cc syringes and 20 gauge needles, both rinsed with physiological saline, were used for venapuncture. The sample was not used if the puncture was not immediately successful. At least 10 cc of blood were drawn for each determination. One cc of blood was run into each of 4 of the coagulation tubes, which were placed in a water bath at 28°C. The tubes were tilted at approximately 3-minute intervals, until they could be inverted without loss of contents. The average time of the 4 tubes was used as the coagulation time of the sample. The normal coagulation time by this method is 6 to 12 minutes.

The oxalic acid solution contained 1 mg of oxalic acid C.P. per cc of distilled water. The solution was sterilized by autoclaving at 15lb pressure for 20 minutes. The Koagamin and Koaginol were obtained from Dr. Steinberg and given according to his directions.

Report of Cases. Table I shows the effect of oxalic acid on the coagulation time of 3 of the 5 cases studied. The dosage varied from 10 to 27 mg daily given intravenously. No reduction in the coagulation time was obtained in any of these 3 cases.

Figs. 1 and 2 are graphic representations of the ineffectiveness of the oxalic acid therapy. The average daily dose in Case 5 (Fig. 2) was 47 mg. Case 4 developed a hemorrhage in the forearm on the first day of oxalic acid therapy which progressed under continued oxalic acid administration. Figs. 1 and 2 also show that these patients are typical in their response to agents which are usually effective in reducing the coagulation time in hemophilia. Attention is called to Fig. 2, which shows the effectiveness of lyophilized human plasma in reducing the coagulation time in hemophilia. Details of this form of therapy will be given in a later publication.

Table II shows the failure of Koagamin and Koaginol to reduce the coagulation time in Case 5. Similarly, no reduction in the coagulation time was obtained in Case 1 after the intravenous injection of Koagamin.

TABLE I.
Effect of Oxalic Acid Intravenously on the Coagulation Time in Hemophilia.

Case No.	Oxalic acid mg per day I.V.	Duration of treatment days	Coagulation time in minutes					Comments
			Control	Days after treatment				
				1	2	3	4	
1	10	5	67	57	63	64	64	Bled for 3 days from vena puncture third day.
2	12	3	67	75		65		
3	27	3	86	81	84	82		

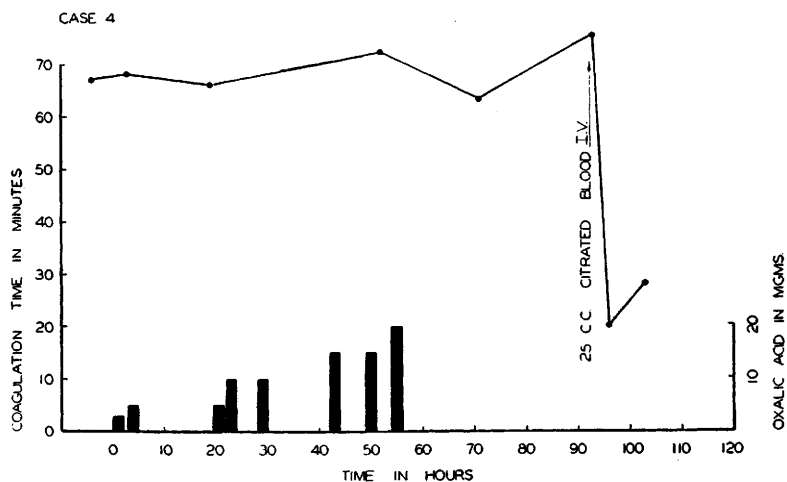


FIGURE I EFFECTS OF OXALIC ACID INTRAVENOUSLY ON COAGULATION TIME IN HEMOPHILIA

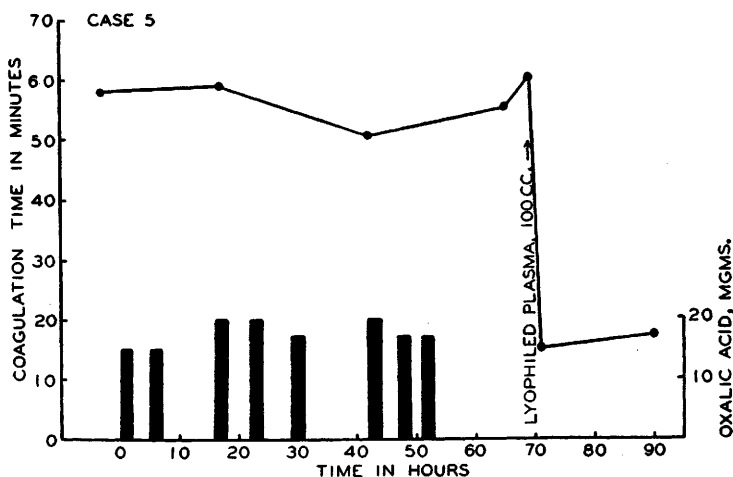


FIGURE II. EFFECT OF OXALIC ACID INTRAVENOUSLY ON COAGULATION TIME IN HEMOPHILIA

Discussion. Our results indicate that oxalic acid in doses from 10 to 47 mg daily by vein, causes no reduction in the coagulation time in hemophilia. Patients from 4 different families have been studied in order to avoid any unusual type of response peculiar to a given family.

We are unable to explain the negative results in our cases as compared with those of Page, *et al.* The fact that they drew only one cc of blood for each test may be one of the factors. We have

TABLE II.
Effect of Koagamin and Koaginol on Coagulation Time in Hemophilia.
Case 5.

Date	Time	Medication	Coag. time, min
9/27		Control	85
9/28		"	88
9/29	8:40 A.M.	Koagamin { 3 cc I.V.	
		Koagamin { 2 " I.M.	
9/29	9:40 "	" 2 " I.M.	99
9/29	10:40 "	" 2 " I.M.	
9/29	11:40 "	" 2 " I.M.	
9/29	2:40 P.M.		97
9/30	2:10 "	" 5 " I.V.	
9/30	4:35 "		100
9/30	4:38 "	Koaginol 2 " I.M.	
10/1*	10:00 A.M.		106

*Large hematoma at site of Koaginol injection.

found this an unreliable procedure as small amounts of tissue juice will materially change the coagulation time when only one cc of blood is withdrawn. We have no explanation for the negative results with the use of Koagamin and Koaginol.

Conclusion. The intravenous injection of Koagamin and oxalic acid in the doses used in this study had no effect on the coagulation time in 5 cases of hemophilia.

Grateful appreciation is expressed to Dr. John Lawrence for criticisms and suggestions.

APPENDIX.

- Case 1. Unit No. 27018. Male. Age 41. Family history of hemophilia. One brother with hemophilia. Has had numerous episodes of hematuria and joint hemorrhages. Has several ankylosed joints. Blood calcium, fibrinogen, and prothrombin time, normal.
- Case 2. Unit No. 86680. Male. Age 12. One of 3 hemophiliacs of present generation. Family history of hemophilia. Has joint hemorrhages (repeated) and many prolonged episodes of bleeding from minor injuries.
- Case 3. Unit No. 27899. Male. Age 43. History similar to that of brother, Case 1. Hemorrhagic episodes dating from infancy through present time.
- Case 4. Unit No. 9987. Male. Age 20. Family history of hemophilia. Has had repeated joint hemorrhages. First episode of hemorrhage at 9 months. Excessive bleeding from minor injuries since infancy. Blood calcium fibrinogen normal.
- Case 5. Unit No. 77669. Male. Age 26. Family history of hemophilia. First hemorrhages at 3 weeks of age. Later severe hemorrhage after circumcision. Repeated episodes of hemorrhage into G.I. tract, joints, and muscles. Several episodes of hematuria, epistaxis, and laryngeal hemorrhage. Blood calcium, fibrinogen, and prothrombin time, normal.