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The effect of sodium citrate on blood coagulation in hemophilia.

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The question of the effect on blood coagulation of the injection of sodium citrate into the circulation was raised immediately after the introduction of the citrate method of obtaining blood for transfusion.

Weil found that in cases with normal coagulation, the coagulation time immediately after citrate transfusions was slightly shortened instead of lengthened. As the question is one of particular importance in the hemorrhagic diseases and as there have been no observations recorded on the ultimate effect of citrate administration on the coagulation of blood, I wish to present some experiments in a case of hemophilia, whose prolonged coagulation time made it particularly suitable for this study.

The patient, an adult male, had nearly bled to death at least six times and presented all the typical features of the disease excepting the family history. The blood count showed nothing abnormal and the blood platelets were within the normal range or slightly above it (490,000 per cu. mm. counted in metaphosphate solution in a counting chamber). The coagulation time of his blood obtained at various intervals within the preceding three years had always been between one and two and a half hours.

The method of determining the coagulation time consisted in obtaining approximately three cubic centimeters of blood with a hollow needle direct from an arm vein. The blood was received into a clean five cubic centimeter test tube and observed at regular intervals, being kept at approximately body temperature. Complete coagulation was recorded when it was possible to turn the tube up-side down without the blood flowing. Beginging or partial coagulation was noted by the retarded flow of the blood when the tube was slanted. This method is far preferable to all the methods which involve the taking of drops of blood from the finger or ear as these methods, due to the admixture of fluids

from subcutaneous tissues, give notoriously inaccurate results. With the present patient on several occasions, blood so obtained and examined in capillary tubes coagulated in from ten to forty minutes at times when the venous blood was known to coagulate in one to two hours.

The injection of 150 cubic centimeters of normal blood from another person mixed with 0.3 gram of sodium citrate shortened the coagulation time of the patient's blood taken ten minutes after the transfusion from one hour fifteen minutes (beginning coagulation at fifty minutes) to seventeen minutes (beginning coagulation twelve minutes). Twenty-four hours later, however, the coagulation time was found to be practically the same as before the transfusion, namely one hour fifteen minutes for complete coagulation (beginning coagulation forty-five minutes). The coagulation time of blood obtained nine days later was one hour, thirty-five minutes (beginning coagulation one hour and twenty minutes).

The intravenous injection of 0.6 gram of sodium citrate (20 cubic centimeters of 3 per cent. citrate solution) shortened the coagulation time of the blood obtained ten minutes after the injection from one hour thirty-five minutes (one hour twenty minutes beginning coagulation) to twenty-five minutes. Forty-eight hours later, however, the coagulation time was found to have been lengthened out to two hours and fifty minutes (beginning coagulation one hour and twenty-five minutes).

At this time when the coagulation of the blood was at its longest, an experiment was made to see whether there was any immediate effect of citrate on coagulation after the citrate was injected into a muscle. The result was negative; the coagulation time taken thirty-five minutes after the intragluteal injection of 0.72 grams of sodium citrate was two hours and fifty-three minutes (beginning coagulation two hours). The coagulation time of the patient was not determined again for two weeks when it was found to have returned to approximately the same level as had been usual before the citrate injections, namely one hour (beginning coagulation forty-five minutes).

The citrate injections and the blood transfusion produced no ill effects whatever. The patient continued to have occasional

slight ecchymoses as before. Two months after the citrate injections he had another one of his attacks of severe hemorrhage.

CONCLUSIONS

I. In hemophilia the intravenous injection of sodium citrate produces an immediate and great shortening of coagulation time which is followed, twenty-four to forty-eight hours later, by a return of coagulation time to its former prolonged period, or by a much greater prolongation of coagulation time than before.

II. The intramuscular injection of sodium citrate seems to have practically no immediate effect on coagulation time.

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The influence of intravenous injections of magnesium sulphate upon the activities of the center of deglutition.

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In order to understand our experimental results the following physiological facts have to be recalled. Three different phenomena which are under the reflex control of the center of deglutition must be distinguished: (1) The transmission of food from the mouth through the pharynx into the esophagus. This is a complex process which comprises the execution, in a coördinate and stable manner, of three separate activities: the closure of the entrances into the post-nasal cavity and into the larynx, and the rapid transportation of the contents of the mouth into the proper direction. We shall designate the entire action as the *initial act of deglutition.* The reflex mechanism which controls it, is more resistant to anesthesia than the two reflex mechanisms of the phenomena to be mentioned next. (2) The peristaltic movements of the esophagus. This is dependent only upon the occurrence of the first mentioned mechanism, the initial act of the deglutition, and is *independent* of the actual passing of some contents through the esophagus or of the anatomical continuity of the latter. Transection of the esophagus or complete removal of a