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

great part of it does not prevent the contraction in the lower part of the esophagus or of the cardia in due time after the initial deglutition, a time which varies with different species of animals (Mosso, Kronecker and Meltzer). The initial sensory impulse, after reaching the center of deglutition, passes consecutively through a number of sections of that center, sending, while thus passing, motor impulses to the corresponding sections of the esophagus. This reflex mechanism of *primary peristalsis* (Meltzer) is very resistant to fatigue, but is less resistant to anesthesia than any other of the reflexes with which we are here concerned. (3) Local reflexes of *secondary peristalsis* (Meltzer). A mechanical stimulus applied to any part of the mucosa of the esophagus (distension) will cause a contraction of the corresponding part of that canal, and, if this stimulus is brought about by some movable mass within the lumen of the esophagus, this mass will be driven down into the stomach by a wave which is difficult to distinguish from a wave of primary peristalsis. If the mass is mechanically prevented from being moved downward, no contraction takes place at any other part of the esophagus below the stimulating mass. That the secondary peristalsis is due to a central reflex and not to a peripheral mechanism, is proven by the fact that it disappears as soon as the vagi are cut. This central reflex is readily fatigued, but is, on the other hand, more resistant to central anesthesia than the transmission of the impulse from section to section within the center.

For several years we were engaged, at various times, in bringing forward evidences for the central nature of the inhibitory action of magnesium salts. With this object in mind, we studied in the present series of experiments the action of these salts upon the primary and the secondary peristalsis of the esophagus. The animals, dogs, received for anesthesia, three milligrams of morphin per kilo body weight. This permitted the operative procedures needed for our experiments, which consisted in exposing the trachea and making a window in it below the larynx; the transection of the esophagus and tying a glass tube in the upper end of it, the exposing of one superior laryngeal nerve and of tying a cannula in the external jugular vein. A short time after the operation the initial act of deglutition could be brought on by either of the three

following methods: by tickling the pharynx with a probe introduced through the window in the trachea, by injecting water or saline solution into the pharynx by the same route, or by electrical stimulation of the superior laryngeal nerve. The occurrence of peristaltic or local contractions of the various parts of the thoracic esophagus were observed by means of a catheter introduced into the stomach end of the esophagus. The catheter had around its esophageal end a small balloon of thin rubber; its outer end was connected with a water manometer. Magnesium sulphate was used in M/4 solution and was infused into the jugular vein from a Mariotte burette.

We shall report now our results very briefly. Before magnesium was given each initial act of deglutition was followed, as a rule, by a primary peristaltic contraction of every part of the thoracic esophagus. Further, stimulation of the esophagus, by moving of the catheter within the esophagus to a new place, or by a temporary distension of the balloon by air, brought on, as a rule, several consecutive contractions of the part in which the balloon was located (secondary peristalsis).

Some time after magnesium was permitted to run into the jugular vein we met first a phase in which the primary peristalsis disappeared, that is, no contraction of any part of the thoracic esophagus was observed to follow the initial act of deglutition. During this early stage the secondary peristalsis was in nearly all cases still present and quite normal; nor was the primary act of deglutition noticeably affected. When, however, more of the solution was infused, a stage was encountered in which also the secondary peristalsis was practically gone, while the initial act of deglutition was still only moderately weakened, and stimulation of the vagus still caused a fairly good contraction of the esophagus. A still further inflow of the magnesium solution finally greatly weakened, or even completely abolished, the initial act of deglutition also.

From these observations it is evident in the first place, that the first effect of the magnesium consists in a weakening or complete abolition of the primary peristalsis, which means that the inhibitory action of magnesium was exerted during this first phase exclusively or essentially upon the transmission of the sensory

impulse from section to section within the center of deglutition. The occurrence of efficient initial acts of deglutition and the presence of the secondary peristalsis testify that during this early stage the local reflexes within the center controlling the primary act of deglutition and the secondary peristalsis are little affected. This is in harmony with the fact that the mechanism in control of the two mentioned local reflexes are more resistant to anesthesia than the mechanism which controls the primary peristalsis. In the second phase also the local reflexes, controlling the secondary peristalsis, are abolished, while the initial act of deglutition is still fairly active. In this phase stimulation of the vagus causes a fairly good contraction of the esophagus. The facts observed during this phase permit the following two conclusions: (I) That the inhibitory action of magnesium in this phase is exerted essentially on the center and but little, if any, upon the motor nerve endings, and (2) that the local reflex of secondary peristalsis, which comes only occasionally into play, is more readily affected than the local reflex of the mechanism of the initial act of deglutition which is frequently in action and which has to be of a stable and resistant character. In the third phase, when the initial act of deglutition is also abolished, the inhibitory action of magnesium is probably exerted upon the center as well as upon the motor nerve endings. For our present purpose, however, it is of no interest to us to analyze the conditions prevailing during this phase.

The chief results of our experiments, so far as the action of magnesium is concerned, consists in the following conclusions: that a graded intravenous injection is capable of causing a complete central depression of the mechanism of deglutition before a peripheral effect can be ascertained; that the transmission of impulses from section to section *within* the center is more readily affected than reflex actions, and that reflexes of an important function in frequent action are more resistant than local reflexes of an incidental character.