while in cases of active infantile tetany it is

$$\frac{327 + 24.9}{5.8 + 2.1} = 44.5.$$

If the calcium were to remain the same, the ratio would be 27.8. It is therefore evident that the change in the ratio of (Na + K)/(Ca + Mg) is due almost wholly to the decrease in the concentration of calcium.

129 (1711)

Serumtherapy of advanced botulism.

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In the course of a series of investigations designed for the purpose of establishing the path of absorption of botulinus toxin in guinea pigs, a number of animals were kept under ether for the purpose of surgical manipulation. It was observed that in such animals death following the introduction of toxin was greatly delayed. Whereas normal guinea pigs of 350 grams given 50,000 minimal lethal doses[1] of botulinus toxin intraperitoneally show symptoms of dyspnea in one hour and invariably die in about two hours, guinea pigs similarly injected but put under ether anesthesia for two hours as soon as dyspnea occurs (*i.e.*, one hour after the injection of toxin) will survive for four hours and by prolonging the period of anesthesia, the life of the animals can be correspondingly prolonged.

We thought that advantage could be taken of this delay in the rate of the progress of the intoxication under ether anesthesia to permit toxin antitoxin combination to take place. Two series of guinea pigs were given 50,000 minimal lethal doses of botulinus toxin per os. Guinea pigs thus fed show first symptoms of intoxication in about six hours and die in about twelve hours. After six hours the first series received antitoxin intravenously while the second series was given antitoxin in a similar manner but at the

[1] The minimal lethal dose used throughout this paper is the amount that is necessary to kill a mouse of 15 grams in less than four days by intraperitoneal injection.

same time put under ether anesthesia which was continued for two hours. The pigs in the first series died in eighteen hours while those in the second series survived.

Further experiments are being carried out which attempt to gain an insight into the nature of the phenomenon, how far it can be applied with relation to other toxins and the effect of other anesthetics. The quantitative and time relationships are also being studied.

130 (1712)

The composite nature of botulinus toxin.

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As we will show in detail in another paper, the lethal dose of botulinus toxin by the mouth is roughly 1,000 removed from that sufficient to kill by the intraperitoneal route. This relation seems to hold true for all the laboratory animals which we investigated, including birds, and is responsible for the failure of certain investigators to kill birds by feeding even large quantities of weak toxin.

In attempting to purify the toxin by precipitation, we were surprised to find that, whereas the purified toxin retained its full potency when tested by injection, it became 100 times less toxic by mouth. In general the further the purification was carried, the greater was the loss in potency of purified toxin when tested by mouth. We have been able to reëstablish the toxicity (by mouth) of such purified toxin by merely adding to it the substances removed by the process of purification.

Since the potency of our purified botulinus toxin as tested by injection remains the same, whereas the toxicity by mouth varies according to the degree of purification of the toxin, it seems to us that the power of crude botulinus toxin to be absorbed through the intestine is dependent upon the presence of secondary substances mixed with the true botulinus toxin.