excess of a fatal dose and which undoubtedly would have killed every one of these animals in less than an hour.

The method which we have employed consists (1) in instituting and keeping up artificial respiration by the continuous insufflation method; (2) in the intravenous administration of curarin from time to time in doses sufficient to control the convulsions; (3) in the injection of a small dose of atropin to meet the slowing of the circulation, and (4) in the infusion of a liberal quantity of Ringer's solution.

Against the fourteen survivors we had thirteen failures. An analysis of these failures, however, shows, first, that in most of these cases the insufflation was improperly adjusted or prematurely discontinued; second, that these animals received only a small quantity of Ringer's solution and in some instances no atropin. In other words, in the failures the method was not properly carried out. We, therefore, believe that we have good reasons for the hope that the above described method, when carried out properly, will prove successful in most cases of strychnin poisoning.

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Intracellular proteolytic enzymes of liver.

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The influence of reaction upon autolysis of animal tissues has been exhaustively studied. All observers agree upon the favorable influence of a weak acid medium, and upon the inhibitory effect alkaline reaction. As an example of the influence of reaction upon autolysis, 2.5 grams of liver after five days at 37 degrees yield the following equivalents of ammonia by the Kjeldahl method; in 0.4 per cent. acetic acid, 35.6 cubic centimeters N/10 H_2SO_4; in 0.2 per cent. acetic acid, 34.8 cubic centimeters N/10 H_2SO_4; in neutral, 11.3 cubic centimeters N/10 H_2SO_4; in 0.2 per cent. sodium carbonate, 4.8 cubic centimeters N/10 H_2SO_4; and in 0.4 per cent. sodium carbonate, 0.6 cubic centimeter N/10 H_2SO_4.

When normal liver is allowed to stand on ice for many days, the power to digest in alkaline medium increases markedly from

week to week until finally the enzyme solution is more active in alkaline than in acid medium. For instance, 2.5 grams of fresh liver after five days autolysis yields an equivalent in 0.2 per cent. acetic acid, of 29.4 cubic centimeters N/10 H_2SO_4; in neutral of 7.9 cubic centimeters N/10 H_2SO_4; and in 0.2 per cent. sodium carbonate, of 2.0 cubic centimeters N/10 H_2SO_4; whereas after standing fifty-five days on the ice the same liver gives in 0.2 per cent. acetic acid 17.6 cubic centimeters N/10 H_2SO_4; in neutral 21.7 cubic centimeters N/10 H_2SO_4, and in 0.2 per cent. sodium carbonate 24.2 cubic centimeters N/10 H_2SO_4. This rise of autolytic activity in neutral and alkaline media is analogous to the rise of tryptic activity of pancreatic extracts on standing, and is probably attributable to the slow conversion of an alkaline digesting enzyme from an inactive into an active form.

Activation of the alkaline enzyme can be accomplished more rapidly by pretreatment of fresh liver with weak acetic acid, a method first used by Hedin in demonstrating the alkaline enzyme of spleen. Two and a half grams of fresh untreated liver after five days autolysis at 37° C. yields an equivalent in 0.2 per cent. acetic acid, of 34.8 cubic centimeters N/10 H_2SO_4; in neutral, of 12.8 cubic centimeters N/10 H_2SO_4; and in 0.2 per cent. sodium carbonate, of 7.7 cubic centimeters N/10 H_2SO_4. The same liver, treated with 0.4 per cent. acetic acid for twenty-four hours on ice, gives after neutralization of the acid, equivalents in 0.2 per cent. acetic acid, of 22.5 cubic centimeters N/10 H_2SO_4; in neutral, of 17.2 cubic centimeters N/10 H_2SO_4; and in 0.2 per cent. sodium carbonate, of 16.8 cubic centimeters N/10 H_2SO_4. Previous treatment of fresh liver with alkali results in the destruction of practically all proteolytic activity. Two and a half grams of liver, treated for twenty-four hours on ice with 0.4 per cent. sodium hydrate, yield, after neutralization, an equivalent in 0.2 per cent. acetic acid, of 3.9 cubic centimeters N/10 H_2SO_4; in neutral, of 0.4 cubic centimeter N/10 H_2SO_4; and in 0.2 per cent. sodium carbonate, of 0.1 cubic centimeter N/10 H_2SO_4. There is some reason to believe that the inactivity following pretreatment of liver with 0.4 per cent. sodium hydrate does not represent destruction of the proteolytic enzymes, but is due to the fixing of the enzyme in the inactive state in which it exists in the cells. When fresh

pancreas is pretreated with sodium hydrate, the same type of inactivity results as is observed in like treatment of liver. This inactive pancreatic extract can readily be activated, however, by the addition of enterokinase. Furthermore, when liver, which has become active in alkaline medium by standing is treated with 0.4 per cent. sodium hydrate, inactivity which occurs when fresh liver is so treated is not produced.

In contrast to the effect of alkaline treatment upon the proteolytic enzymes of liver and pancreas is its effect upon the alkaline digesting enzyme of the polymorphonuclear leucocyte. It has been observed that the leucoprotease of the polymorphonuclear leucocyte maintains its activity when kept continuously in alkaline medium, and is able to effect proteolysis after treatment with sodium hydrate. From this observation it seems probable that leucoprotease exists in the cell in an active form.

The work outlined leads to the following conclusions. Autolysis of fresh normal liver progresses much more favorably in acid than in alkaline medium. Allowing liver to stand, and treating liver with weak acetic acid call into activity an enzyme which shows marked proteolysis in alkaline medium. This enzyme exists in the cell in an inactive form. Liver probably contains two proteolytic enzymes, one acting in acid and the other in alkaline medium. The inhibitory effect of alkali upon liver autolysis is referable to the preservation of the zymogen condition of the enzyme which acts in alkali. The maintenance of the equilibrium of the proteolytic enzymes of liver must be intimately dependent upon the preservation of tissue neutrality. The fact that leucoprotease is active after pretreatment with alkali suggests that this enzyme exists in the cell in an active form.

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Enzymes and antienzymes of the blood serum with certain degenerative changes in the liver.

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Since the liver undergoes advanced degenerative changes with chloroform poisoning it is possible that proteolytic enzymes are set