

ON ABSORPTION OF STRYCHNINE AND HYDROCY-
ANIC ACID FROM THE MUCOUS MEMBRANE OF
THE STOMACH.—AN EXPERIMENTAL
STUDY ON RABBITS.*

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It has always been, and still seems to be, the prevailing opinion that the stomach is capable of absorbing soluble and diffusible substances, and there seemed, indeed, to be no reason to suppose that the mucous membrane of the stomach should with regard to absorption be inferior to any other mucous membrane.

Recent investigations, however, have brought to light some new facts with regard to the power of absorption of the stomach, the most striking of which is surely the unexpected result that the stomach does not absorb any water. Edkins † introduced into the stomach of cats, after the ligation of cardia and pylorus, a measured quantity of salt solution, and recovered after an hour exactly the same quantity again. Von Mering, ‡ who experimented on dogs with a duodenal fistula, found that a larger quantity of water came out through the fistula than the dogs had taken by the mouth. As my experiments have reference mainly to the absorption of strychnine and of hydrocyanic acid, I shall restrict my references to literature to those having direct bearing upon this subject. As far as I can ascertain,

* Read at the Eleventh Annual Meeting of the Association of American Physicians, April 30, 1896.

† J. S. Edkins, The Absorption of Water in the Alimentary Canal. *Journal of Physiology*, 1892, p. 460.

‡ Von Mering, Ueber die Functionen des Magens. *Therapeutische Monatshefte*, Mai, 1893.

there are only two statements on the absorption of strychnine in the stomach.

Bouley and Colin * have introduced strychnine into the stomach of animals whose pylorus was either ligated or paralyzed by vagotomy. They report that in the dog, swine, and cat the effects of the strychnine appeared very rapidly; the effect was retarded in the cow, and there was no effect—at least, no fatal effect—in the horse. Tappeiner † has experimented with strychnine exclusively upon cats, in whose stomach the poison was introduced through a stomach tube. A normal cat of about 2 kilos succumbed to the effects of 0.03 gramme of strychnine in an aqueous solution in eight minutes; cats whose pylorus was tied succumbed to doses of 0.05 and more only after an hour and thirty minutes or even later. If the strychnine solution, however, contained some alcohol, the strychnine took effect almost as rapidly as when the pylorus was not tied. Tappeiner also found that chloral hydrate in aqueous solution was not absorbed in the stomach of a dog with closed pylorus, while an alcoholic solution of it was readily absorbed.

Concerning the absorption of prussic acid from the stomach, I could find no reference.

My experiments relate to the absorption of various solutions in dogs and rabbits, and also in frogs, but I shall report here only the results I obtained in rabbits with strychnine nitrate and hydrocyanic acid. The animals were all well narcotized with ether during the operation. In most cases, after the introduction of the poison into the stomach, the pyloric and cardiac ends of the stomach were tied. At the pylorus the ligature was applied in the groove between the pylorus and duodenum, avoiding the inclusion of the vessels of the stomach, and at the cardia the ligature was applied on the oesophagus just beneath the diaphragm. I shall now let the experiments speak for themselves.

EXPERIMENT 3.—Rabbit, 1,800 grammes, not starved. Through a soft catheter, introduced by the mouth into the stomach, 10 milli-

* Colin, *Traité de physiologie comparée*, vol. ii, p. 91.

† Tappeiner, *Ueber Resorption im Magen. Zeitschrift für Biologie*, 1880.

grammes of strychnine were injected, catheter removed, and rabbit taken off from the board. After fourteen minutes a typical strong tetanus broke out; a few more followed, and the rabbit died.

EXP. 41.—Rabbit, 1,760 grammes, not starved. Through an opening made in the œsophagus a catheter was introduced into the stomach, and 6 milligrammes of strychnine in water coloured with methylene blue injected. Rabbit put on a box. After eighteen minutes, animal showed great uneasiness, and nine minutes later, with a sudden jerk, a strong opisthotonos set in, which lasted over two minutes. Rabbit remained hyperæsthetic for half an hour, and gradually recovered.

These two control experiments are sufficient to show that 6 to 10 milligrammes of strychnine brought into the full stomach of a rabbit do not fail to produce within half an hour the characteristic effect.

EXP. 4.—Rabbit, 980 grammes, starved three days, stomach nearly empty. Cardia tied, an opening made in duodenum, and a thin catheter introduced into the stomach, reaching the wall of the fundus. Sixty milligrammes of strychnine in 10 cubic centimetres of a forty-per-cent alcoholic solution, coloured with indigo carmine, were injected, the tube removed, duodenum and abdomen sewed up, and the animal brought to the box. The rabbit lived fifteen hours, and at no time was there any sign of hyperæsthesia, of increased reflex irritability, not to speak of a convulsion. The death was apparently due to peritonitis and aspiration pneumonia (“Schluckpneumonie”), but certainly not to strychnine poisoning. The stomach was considerably distended, and apparently contained more fluid than before the ligation.

It might be claimed that the explanation of the striking fact that 60 milligrammes of strychnine could remain for fifteen hours in the stomach without absorption is that by the ligation of the cardia and pylorus all the blood vessels and the lymphatics of the stomach were ligated, thus leaving no path open by which the poison could have been carried into the circulation. However, the stomach had by no means an ischæmic appearance; on the contrary, distinct pulsation could be seen also after the ligation, and the stomach retained in every respect its natural appearance. At any rate, such a claim can not be raised against the following experiment.

EXP. 7.—Middle-sized rabbit, pylorus ligated, cardia open; introduced through a catheter by the mouth 60 milligrammes of strychnine

in an aqueous solution. Rabbit lived nineteen hours without showing any effects of strychnine. Death and autopsy as in the preceding experiment.

Here the vessels of the cardiac end of the stomach remained open; nevertheless no absorption took place.

Exp. 28.—Rabbit, 1,200 grammes, starved two days, cardia left open; introduced a tube through the duodenum into the stomach; injected into the fundus 45 milligrammes of strychnine; rabbit remained for an hour on the holder; no sign of any effect. Then the rectum was tied, and by a hypodermic syringe $3\frac{1}{2}$ milligrammes of strychnine, coloured with indigo carmine, were injected through the wall of the rectum into the impacted lumen. After twelve minutes a tetanic outbreak set in, which terminated fatally. The tetanic outbreak was apparently due to the quick absorption of the $3\frac{1}{2}$ milligrammes of strychnine from the rectum. No drop escaped into the peritoneal cavity or infiltrated the wall of the rectum, as could be seen by the absence of the blue colour.

Against the conclusion that the mucous membrane of the stomach of the rabbit does not absorb strychnine, another objection could be raised, namely, that the stomach of the rabbit is never thoroughly empty, and that the strychnine in all the cases is enveloped by the remnants of the food and does not come in contact with the mucous membrane at all. To meet this objection, the following experiment was made:

Exp. 35.—Rabbit, 1,200 grammes, starved sixty hours, stomach quite empty. By a catheter, which was introduced through an opening in the œsophagus, 100 cubic centimetres of water were brought into the stomach, catheter removed, and cardia left open. A tube was introduced through duodenum and pylorus; the inner end of this tube was brought in close proximity with the wall of the stomach, then 60 milligrammes of strychnine, deeply coloured with indigo carmine, was injected, and some air blown in; now the tube was removed and the pylorus tied. An hour and twenty minutes passed by without a sign of a strychnine effect. Judging from the manifold experiences I had had I was sure that if the rabbit did not show the effects of the strychnine in the first hour the effect would not appear at all. Therefore the rabbit was used for another experiment. Three milligrammes of strychnine were

injected through the anus into the rectum. After eight minutes a brisk tetanus carried the rabbit off. At the autopsy the entire stomach was taken out. The stomach was transparent, the level of the fluid was distinctly visible and changed easily with each change in the position of the stomach. On opening the stomach, the contents flowed out easily, no food clung to the mucous membrane, and where the coloured strychnine touched the mucous membrane there were distinct marks of the indigo carmine superficially adherent to the epithelial layer.

In this experiment the strychnine was surely in close contact with the mucous membrane of the stomach, and the vessels of the cardiac end were also not ligated; nevertheless no absorption took place.

EXP. 40.—Rabbit, 2,100 grammes, cardia tied; tube passed through duodenum into the pyloric part of the stomach; injected 50 milligrammes of strychnine, coloured with indigo carmine, directed to the front wall of the pyloric part; this part bulged up, tube removed, and pylorus tied. After two hours and five minutes, still no effect. Now 5 milligrammes of strychnine, coloured with methylene blue, was injected into the front wall of the stomach between the muscularis and the mucosa; a blue-stained area appeared, but no drop of the fluid escaped. After two minutes, a stormy tetanus broke in like lightning, and the rabbit was dead.

This shows strikingly that the ligation of the cardiac and the pyloric ends of the stomach does not prevent in the slightest the lymphatics and the blood vessels from carrying into the circulation the fluid which reaches them.

In sharp contrast to our results with strychnine, we found that the stomach of the rabbit promptly absorbs prussic acid.

EXP. 6.—Large rabbit, not starved, cardia tied; tube introduced through the duodenum into the stomach; injected 100 milligrammes of hydrocyanic acid (5 cubic centimetres of the official two-per-cent solution), coloured with indigo carmine; tube removed and pylorus tied. Rabbit soon shows uneasiness, the breathing becomes laboured, clonic convulsions set in, and the animal dies in fifteen minutes.

EXP. 26.—Rabbit, 2,200 grammes, not starved, cardia ligated; tube passed through duodenum; injected into the fundus 60 milligrammes of

prussic acid; tube removed and pylorus tied. Rabbit dies after twelve minutes in the same manner as in the former experiment.

At the autopsies of some of the rabbits which died from prussic acid, distinct hæmorrhagic surfaces were found on the mucous membrane of the stomach. This probably accounts for the good absorption of the prussic acid. The fact that hydrocyanic acid was constantly absorbed from the ligated stomach of the unstarved rabbits shows that the acid easily reaches the mucous membrane even in a full stomach, and, further, that the ligation alone does not prevent the blood vessels and the lymphatics from absorbing fluids which come within their reach. I have, therefore, in a few experiments with strychnine used the absorption of hydrocyanic acid as a test for the points in question.

Exp. 12.—Very large rabbit, 3,200 grammes, starved twenty-four hours, cardia tied; introduced tube through duodenum into the stomach, and pylorus tied tightly around tube. At 5.12 p. m. injected 50 milligrammes of strychnine in 10 cubic centimetres of water; at 8.28 rabbit perfectly quiet; injected again 50 milligrammes in 10 cubic centimetres of alcohol (fifty per cent). At 9.28 rabbit sleeps well; no sign of strychnine effect. Injected now 100 milligrammes of prussic acid in an alcoholic solution; rabbit soon starts breathing irregularly; short inspirations; convulsive expirations, with long intermission; heart first slow, then very rapid, growing imperceptible; some clonic convulsions; no hyperæsthesia; no tetanic or tonic contractions; rabbit dies gradually within twenty minutes.

Exp. 42.—Rabbit, 1,740 grammes, cardia tied; tube through duodenum into stomach; injected 200 milligrammes of strychnine in 20 cubic centimetres of water; tube removed and pylorus tied. After an hour and fifty minutes no effects whatsoever; 60 milligrammes of prussic acid, coloured with methylene blue, were now injected by means of a hypodermic needle, thrust through the front wall of the stomach, directly into the mass of food; the fine opening clamped; nothing escaped. Very soon after the veins on the walls of the stomach present a bright brick-red colour; the same was seen on the edges of the spleen; irregular laboured breathing set in; some clonic convulsions appeared without the presence of any hyperæsthesia; the rabbit died within twelve minutes.

The death was certainly due to the prussic acid, which rapidly reached the mucous membrane, penetrated it, and was carried off by the lymphatics and the blood vessels into the circulation. The enormously large dose of strychnine has probably also reached the mucous membrane, and would also have been carried into the circulation if it could only penetrate the epithelial layer to reach the lymphatics and the blood vessels.

I append two more experiments to show the character of absorption in some other parts of the alimentary canal.

EXP. 23.—Large rabbit, cardia tied; tube passed through duodenum into the stomach; injected 40 milligrammes of strychnine in a thirty-three-per-cent alcoholic solution; tube removed and pylorus tied. After eight hours no effect. Then 14 milligrammes of strychnine were injected into the œsophagus, the upper end of which was tied. After an hour and thirty-five minutes, still no effect. Now 4 milligrammes of strychnine were injected into the pharynx; in four minutes a brisk tetanus broke in, which ended fatally. Of course, it can not be stated whether the absorption has taken place only within the pharynx or also in the mouth, and perhaps even only in the mouth alone, though the injection was made directly into the pharynx.

EXP. 19.—Middle-sized rabbit, œsophagus tied at the upper end and also below the diaphragm. The vagi and the inferior laryngeal nerves were avoided. Through a cannula tied in the œsophagus several injections were made. At first only 4 milligrammes of strychnine were injected; half an hour later 4 milligrammes more were added, and forty minutes after this again 10 milligrammes were injected. An hour and fifteen minutes passed after the last injection with no sign even of increased irritability. Now 4 milligrammes of strychnine were injected into a loop of the small intestine; after seven minutes there was already marked hyperæsthesia, and five minutes later a stormy tetanus caused death.

I have to add that in one experiment half an hour after injection of 10 milligrammes of strychnine into the œsophagus, a tetanic attack did take place, but the œsophagus in this case was very much distended by air, which surely facilitates the absorption.

The results of my experiments, briefly summed up, are as follows:

The introduction of 6 to 10 milligrammes of strychnine into the full stomach of a rabbit with pylorus open is sure to bring on a tetanus within a short time. The effect is probably brought about by the rapid passage of the strychnine from the stomach into the intestine, whence it becomes absorbed in a few minutes.

When the pylorus, however, is closed, even such large doses as 200 milligrammes of strychnine, remaining for many hours within an empty stomach, with good circulation and with intact innervation of the vagi, do not produce any effect at all. It seems that the mucous membrane of the stomach does not absorb even the smallest fraction of the strychnine. Next to the stomach, we also found that the mucous membrane of the œsophagus absorbs strychnine very poorly.

The pharynx is apparently the part of the alimentary canal which absorbs best; 3 to 4 milligrammes in the pharynx will induce a tetanus in three to four minutes.

The rectum absorbs nearly as well as the pharynx, as 3 milligrammes injected through the anus will call forth a tetanus in six to eight minutes. The absorption seems to take place here even better than in the small intestine, as it takes twelve to fifteen minutes before a tetanus breaks out after an injection of 4 to 5 milligrammes of strychnine into a loop of the small intestine.

Prussic acid is absorbed very well from the stomach even when the pylorus is ligated. It seems to produce a hæmorrhagic surface on the mucous membrane, which facilitates the absorption. Possibly, also, the volatility of prussic acid may favour prompt absorption, as gases seem to be readily absorbed in the stomach.