THE ACTION OF SOME MERCURY SALTS ON THE INTESTINE OF THE CAT.

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ABSTRACT.

Mercury salts cause an increase in intestinal movements as a result of irritation to the intestinal mucosa. The intensity of action increases with a rise in concentration. The mercurous require a longer time to produce their effects than the mercuric salts. The increase in the fluid of the intestine is not due to a secretion of succus entericus, since no ferments were detected.

The salts of mercury, such as mercurous chloride (calomel) and mercuric chloride, differ in their actions on the intestine. Calomel, in therapeutic doses, causes no damage to the intestine, while mercuric chloride, in cases of poisoning, irritates the intestinal mucosa. The extent of this varies with the concentration, the amount of the drug taken, and the time allowed for it to act. Calomel, in comparatively big doses, produces no harmful effects. In mercuric chloride poisoning diarrhoea is always a prominent symptom, and the intestinal contents are often blood-stained. This indicates considerable damage to the intestine. The mercuric chloride reaction is more intense than that of calomel, since it is very soluble, not only in water, but also in body fluids and in an excess of protein. Calomel, on the other hand, is comparatively insoluble, but its solubility rises in the presence of sodium chloride, which is present in the intestinal fluid. It seems probable that the ionised mercury is responsible for the purgative action, since mercuric salts are more active than mercurous, and insoluble mercury salts, such as mercury sulphide, are inactive. The solubility of mercuric chloride in water, at 15°C., is 5.73%, and at 100°C., 53.96%. The corresponding solubilities for calomel are 0.00031% and 0.01%. The solubility of calomel

at 37°C. must lie somewhere between these extremes. To test the action of a mercury salt on the intestine, various concentrations of mercuric chloride were selected.

METHOD.

Cats, anaesthetised with chloralose (0.1 g. per kg.) were used. Intestinal loops of 10 to 12 cms. length were prepared as described elsewhere.[1] To keep the temperature of the animal as nearly normal as possible, the lower half of its body was submerged in a bath of Ringer's fluid kept at 37 C. In each cat the loop was filled with measured quantities of 0.9% sodium chloride for obtaining normal movements, and with corresponding quantities of mercury solutions of known concentration, in 0.9% sodium chloride, for comparison. The time allowed for any solution to act was the same in all cases, and was usually limited to fifteen minutes. The fluid recovered at the end of each period was measured to determine whether absorption or secretion had taken place. Only a section of the movements of each period are reproduced in Figure I.

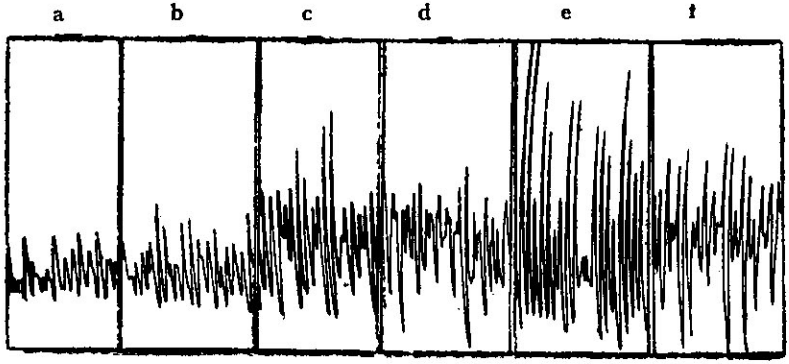

Fig I.

RESULTS.

In Fig. Ia is seen the type of movement obtained from the sodium chloride. Fig. Ib shows the effect of a 0.01% solution

[1]Dreyer, *J. Pharmacol.*, **36**, 477 (1929).

of mercuric chloride, which was taken as the lowest effective concentration. There was a slight but perceptible increase in amplitude but no increase in rate. This solution was replaced by another of double concentration (0.02% $HgCl_2$), (Fig. Ic.) The amplitude is greatly increased and the tone to a lesser extent. On removal of the mercury solution a cloudiness was perceptible in it, and on microscopic examination numerous epithelial cells were found. The intestinal lumen was next washed with 0.9% sodium chloride, to remove as much as possible of the mercury adherent to the mucosa, and the movements were tested after this with the sodium chloride in the intestine (Fig. Id). The intestine showed almost as much activity as when the mercury solution was acting. Increasing the mercury salt concentration to 0.04% a very pronounced increase was observed in the movements, with practically no change in the "diastolic" level of the intestinal movements (Fig. Ie). There seemed to be no diminution in the activity of the intestine as time went on. After washing out the mercury solution and replacing this by the neutral sodium chloride the increased activity of the intestine persisted (Fig. If). These movements were almost entirely peristaltic. Observation of the loop showed that at times the contractions were so strong that the intestine became almost bloodless, and the movements were more of the nature of spasms of the whole length of the loop. The higher concentrations of mercuric chloride produced very severe damage to the mucous membrane. The fluids, on removal, were found to be quite turbid and on standing deposits, consisting of large clumps of epithelial cells, settled out. Occasionally the fluids were blood-stained. Repeated washing of the mucosa with 0.9% sodium chorlde did not restore the motility of the intestine to its initial level. Instead, the increased activity continued for several hours, though not as marked as when the mercury solution was acting on the intestine. This after-effect was probably due to the irritation of the mucosa. With the lower concentrations of mercury the after-effect was not so prominent or even absent

with the minimal effective concentration (0.01%), depending probably on the degree of irritation. It is probable that if a segment in the upper intestine became overactive from mercury stimulation, such a segment acted as a pacemaker for the intestine below. Further, since with therapeutic doses of calomel the mercury is inactivated to sulphide on reaching the lower part of the small intestine and the large intestine, the pacemaker hypothesis may account partly for the stimulant action of mercury salts, in therapeutic doses, on the lower intestine. The power of the intestinal epithelium to absorb fluid is not abolished by the very dilute solutions of mercuric chloride, but the absorption of water is absent with the higher concentrations. It should be pointed out that the increase in fluid in the intestine is not sufficient to account for the great increase in motility, for when known amounts of 0.9% sodium chloride were run in and records of movements were taken. bigger movements due to increased pressure were found, but never to the same degree as when a mercury solution was acting. Further, in animals deprived of water for twelve hours, an increase in movement always followed the application of mercury solutions, without, or with only a slight increase in the volume of fluid. (Table 1). When, however, an increase in fluid does occur, the irritant action of the mercury salt is aided by the increased intestinal pressure. But when precautions were taken to prevent any appreciable rise in pressure, the movements were still increased by the mercury solutions. It will be seen from Fig. If that the irritation of the intestinal mucosa persists, after removal of the stronger mercury solutions, even after a thorough washing of the intestinal mucosa, and that instead of absorption, "secretion" is now present.

The action of calomel on the intestine is milder and is slower in onset than that of mercuric chloride, but once it begins to act, the effects resemble those of the lower concentrations of mercuric chloride. Suspensions of calomel left in contact with the intestinal mucosa for periods lasting from one to two hours cause severe damage to the mucosal cells,

Table 1.

Cat. Chloralose. Vagi, and splanchnic nerves and adrenals intact. Loop of upper jejunum. $HgCl_2$ solutions made up in 0.9% NaCl. Solutions left in for fifteen minutes.

Fluid.	Amount Put in.	Amount Recovered.	
(1) 0.9% NaCl	11.0 c.c.	9.0 c.c.	absorption
(2) 0.01% $HgCl_2$	11.0 c.c.	10.3 c.c.	absorption less than in 1
(3) 0.02% $HgCl_2$	11.0 c.c.	11.6 c.c.	increase in fluid
(4) 0.9% NaCl	11.0 c.c.	10.5 c.c.	absorption
(5) 0.04% $HgCl_2$	11.0 c.c.	11.8 c.c.	increase in fluid
(6) 0.9% NaCl	11.0 c.c.	11.5 c.c.	increase in fluid

and here, too, shreds of mucous membrane can be found in the intestinal fluid. The irritation so produced leads to an increase in the intestinal fluid. The fluids recovered from the intestine following the action of mercury salts contain none of the enzymes characteristic of succus entericus. Repeated tests for erepsin and invertase proved negative. In all cases the mercury was inactivated before testing for ferments. This points to the fact that the increased "secretion" was not one of succus entericus, but was probably of the nature of an exudate.