Brit. J. Pharmacol. (1957), **12**, 104.

THE EFFECT OF ETHER AND PENTOBARBITONE SODIUM ON GASTROINTESTINAL FUNCTION IN THE INTACT RAT

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(RECEIVED NOVEMBER 28, 1956)

The effect of ether and pentobarbitone anaesthesia on gastrointestinal motility and absorption has been studied by measuring simultaneously gastric emptying, small intestinal transit and intestinal absorption of glucose and iodide in intact rats. Both gastric emptying and intestinal transit are very slow under ether anaesthesia, but with pentobarbitone there is no significant delay. The absorption of glucose by the small intestine is significantly impaired by ether but not by pentobarbitone, and a tracer dose of iodide is absorbed normally under both forms of anaesthesia.

Many experiments on gastrointestinal function in animals have been carried out under anaesthesia, but there has been little quantitative work on the effect of anaesthetics on the gastrointestinal tract. Gastric emptying has been studied radiologically after opaque meals (Cannon and Murphy, 1907; Baron and Barsony, 1914; Sleeth and van Liere, 1938; van Liere and Northup, 1941) and pressure changes in the stomach and intestine have been recorded from balloons placed in the stomach or in Thiry-Vella loops (Miller, 1926; Quigley, Barlow and Himmelsbach, 1934; Bisgard and Johnson, 1939; Burstein, 1939; Gruber and Gruber, 1941; Golden and Mann, 1943). Intestinal motility has also been investigated by measuring the distance travelled by a charcoal-acacia meal (Emerson, 1937; van Liere, Stickney and Northup, 1947). The usual experimental animal has been the dog. All authors find some delay in gastric emptying and intestinal motility under ether anaesthesia. Barbiturates have sometimes been said to decrease gastrointestinal motility, but other authors have found little effect.

There is little convincing evidence available on the effect of anaesthetics on intestinal absorption. Some techniques are open to the objection that variations in gastric emptying are not taken into consideration (Heller and Smirk, 1932) and others to the objection that unanaesthetized controls are not available (Valette and Anglade, 1953). Cordier and Chanel (1948) found delayed intestinal absorption of glucose after both thiopentone and ether, but their work is open to the criticism that they estimated gastric emptying from residual gastric glucose, ignoring gastric absorption of glucose (Reynell and Spray, 1956a). Olmsted and Giragossintz (1929) found flat glucose tolerance curves in dogs anaesthetized with amylobarbitone, and these could not be entirely accounted for by delayed gastric emptying.

We have investigated the effects of ether and pentobarbitone sodium on gastrointestinal function using a method by which gastrointestinal absorption and transit can be measured simultaneously in the intact rat (Reynell and Spray, 1956a, b).

METHODS

Adult male rats of the Wistar strain (200 to 400 g. weight) were used. They were starved overnight but allowed water *ad libitum*, and on the following morning each rat was intubated with a gum elastic catheter and 4 ml. of a solution, containing approximately 3 mg. phenol red, 800 mg. glucose, and 2 μc. ^{131}I as sodium iodide of high specific activity, were introduced into the stomach. The animals were divided into the following groups:

Intraperitoneal Pentobarbitone Sodium.—Seven rats were given 12 mg. pentobarbitone sodium in 0.2 ml. by intraperitoneal injection. Anaesthesia was achieved within a few minutes and maintained for 2 hr., after which time the animal was killed. It was usually necessary to give a further injection of 6 mg. pentobarbitone sodium after about 90 min. to maintain full surgical anaesthesia.

Oral Pentobarbitone Sodium.—Six rats were given 24 to 36 mg. pentobarbitone sodium with the glucose and phenol red. In all but one of them this induced

anaesthesia within 10 min., which persisted for 2 hr., when the animals were killed. A further four rats (not included in the series) died under anaesthesia.

Ether.—Twelve rats were kept anaesthetized by open ether for 2 hr. after intubation and were then killed.

Controls.—Nine rats were not anaesthetized but were killed 2 hr. after intubation.

The stomach and small intestine of each rat were divided into the following four segments: stomach, proximal half of small intestine, third quarter of small intestine, and distal quarter of small intestine. Each segment was homogenized and analysed separately for phenol red, glucose, and ^{131}I by the methods of Reynell and Spray (1956a).

Gastric emptying, intestinal transit for each segment of small intestine, estimated intestinal absorption of glucose and of iodide, and % intestinal absorption of glucose and of iodide were calculated as described elsewhere (Reynell and Spray, 1956a, b).

Extent of Gastric Emptying.—This was the amount of phenol red which had left the stomach during the experimental period. It was calculated by expressing the amount of phenol red recovered from the stomach at the end of the experiment as % of the amount recovered from the whole gastrointestinal tract.

Intestinal Transit.—Transit through a segment of small intestine was calculated by measuring the amount of phenol red which had entered the segment during the experimental period and the amount which had passed on to more distal segments during the same period of time. The latter was then expressed as % of the former.

Estimated Intestinal Absorption.—The absorption of glucose or of iodide was found by calculating the amount of test substance which had left the stomach during the experimental period (calculated from the dose given and the gastric emptying) and then subtracting the amount finally recovered from the small intestine.

% *Intestinal Absorption.*—For this quantity, the estimated intestinal absorption of glucose or of iodide was expressed as % of the amount of test substance which had left the stomach during the experimental period.

RESULTS

Gastric Emptying and Intestinal Transit

These results are given in Table I. There were no statistically significant changes in motility under pentobarbitone anaesthesia, although both mean gastric emptying and intestinal transit were slightly slower than in the controls, particularly when the drug was given by intraperitoneal injection. Since these differences were not significant, no attempt was made to assess the effect of inert intraperitoneal injections. Under ether anaesthesia, on the other hand, gastric emptying and intestinal transit were significantly delayed. In no animal did more than 34% of the initial dose of phenol red leave the stomach in 2 hr. In 4 of 12 animals no phenol red had passed beyond the first half of the small intestine, and in only 3 had any entered the distal quarter of the small intestine during the 2 hr. following intubation. In all controls, some phenol red had entered the distal quarter of the small intestine and in 3 some had entered the caecum by the time the animal was killed.

TABLE I

EFFECT OF PENTOBARBITONE SODIUM AND OF ETHER ON GASTRIC EMPTYING AND TRANSIT THROUGH THE SMALL INTESTINE

	No. of Animals	% Gastric Emptying	% Intestinal Transit		
			1st Half	3rd Quarter	4th Quarter
Normal controls	9	66·0 (±5·8)	90·0 (±1·5)	45·6 (±14·1)	12·9 (±9·6)
Pentobarbitone (oral)	6	62·0 (±9·0)	86·0 (±3·2)	55·7 (±7·1)	4·3 (±4·4)
Pentobarbitone (i.p.)	7	53·7 (±5·4)	84.3 (±1·9)	34·3 (±10·7)	0
Ether ..	12	21·3 (±3·2)	35·4 (±9·9)	12·0 (±7·3)	0

The numerals in brackets give the standard error of the mean.

Absorption of Glucose and Iodide

Under pentobarbitone anaesthesia, oral or intraperitoneal, the amount of glucose and iodide absorbed and the % intestinal absorption of each were slightly reduced as compared with controls, but the differences were not statistically significant. The reduction in the amount absorbed was in part due to the rather longer mean gastric emptying time in the anaesthetized animals. Under ether anaesthesia, the amounts of glucose and iodide absorbed were much reduced, but this was due mainly to the delayed gastric emptying. Nevertheless there was a significant reduction (difference/S.E. difference = 3.48) in % intestinal absorption of glucose. The percentage intestinal absorption of iodide was not significantly reduced. Table II records these results.

TABLE II

ABSORPTION OF GLUCOSE AND OF IODIDE IN TWO HOURS BY THE SMALL INTESTINES OF NORMAL AND ANAESTHETIZED RATS

	No. of Animals	Estimated Intestinal Absorption of Glucose (mg.)	% Intestinal Absorption of Glucose	Estimated Intestinal Absorption of Iodide (% of Dose Given)	% Intestinal Absorption of Iodide
Normal controls	9	502·4 (±41·2)	95·8 (±1·1)	59·7 (±5·4)	90·9 (±1·7)
Pentobarbitone (oral) ..	6	469·5 (±76·5)	94·8 (±1·2)	56·0 (±8·3)	89·3 (±1·3)
Pentobarbitone(i.p.)	7	365·4 (±34·5)	89·6 (±2·0)	48·4 (±5·5)	90·0 (±2·0)
Ether ..	12	148·5 (±27)	72·8 (±6·9)	17·8 (±2·8)	83·0 (±2·2)

The numerals in brackets give the standard error of the mean.

Discussion

We have confirmed previous qualitative observations that the emptying time of the stomach and the propulsive motility of the small intestine are much reduced by ether anaesthesia. The capacity of the small intestine to absorb glucose is also impaired. The results do not indicate the mechanism by which these changes are brought about, but Miller (1926) has shown that ether reduces the force and amplitude of intestinal contractions in a denervated Thiry-Vella loop, suggesting that it has a direct peripheral effect on smooth muscle.

We have found slightly delayed gastric emptying and intestinal transit in animals anaesthetized with pentobarbitone sodium, but the results are not significant and the changes can be of little practical importance. Although previous observations on the effect of barbiturates on gastrointestinal motility have been contradictory, some of the differences may have been due to the rate and route of administration. In a careful series of experiments Golden and Mann (1943) showed that a rapid intravenous injection of thiopentone caused transient inhibition of small intestinal motility, but there was no appreciable effect if the drug was given slowly.

We suggest that valid observations on gastrointestinal absorption and motility can be made on anaesthetized animals if pentobarbitone sodium is used, but that ether should be avoided for experiments of this kind, in which anaesthesia is prolonged.

In surgical practice it is recognized that postoperative vomiting and other gastrointestinal disturbances are commoner after ether than after other anaesthetics (Bisgard and Johnson, 1939), and, although operative trauma probably has a greater inhibitory effect on gastrointestinal motility than ether anaesthesia alone (Cannon and Murphy, 1907), ether anaesthesia might summate with other influences in precipitating paralytic ileus.

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