and XXV were tested. Only XI exhibited any activity. When compared to aspirin this activity was insignificant.

Local anesthetic activity was assayed as the ability of the test agent to inhibit the blink reflex in the rabbit when the cornea was lightly stimulated. Butacaine sulfate (Butyn sulfate) was used as a control local anesthetic. Compounds XI, XV, XVI, XX, and XXI were tested and found to have no local anesthetic activity.

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COMMUNICATIONS

Evaluation of an Improved Heidelberg Telemetry Capsule for the Study of Antacids

Keyphrases ☐ Heidelberg FM-transmitting capsule—evaluation ☐ Gastric function assessment—Heidelberg telemetry capsule, evaluation

Sir:

Development of a telemetry system employing the Heidelberg FM-transmitting capsule has provided a convenient methodological approach to the clinical assessment of normal gastric function, as well as disease- and drug-induced alterations in gastric activity. The Heidelberg capsule, while elegant in concept, has been found lacking in dependability, a defect related possibly to transmitter construction. One factor involved in the lack of reliability may have been the relatively large hydrogen-ion sensor that permitted accumulation of particulate matter (*e.g.*, antacids) and mucous debris, thus interfering with normal operation. Furthermore, a relatively high percentage of the capsules did not exhibit a linear response throughout the functional range of pH 1 to 7 during *in vitro* standardization (1).

A modified Heidelberg probe,[1] having a smaller hydrogen-ion sensitive area, has recently been made available. These redesigned telemetry capsules have demonstrated a high degree of *in vitro* reliability with regard to linearity of response in the workable pH range of 1 to 7. The purpose of this study was to evaluate the *in vivo* performance of this modified device.

A FM-signal receiving unit,[1] in belt form, was positioned externally over the stomach area of healthy adult human subjects and connected to a recorder for continuous monitoring of transmitted pH values. Throughout the experimental period the subjects sat erect in an arm chair. Each telemetry capsule was activated by saturation of the hydrogen-ion sensitive end-plate with 0.9% sodium chloride solution, and calibrated in Beckman buffer solutions of pH 2 and 7 at 37°. The capsule was swallowed by the fasted subject, and gastric pH was monitored during the subsequent 50-min. period. After recording baseline pH values (3 to 10 min.), a specified dose of one of four commercial antacid preparations (designated A, B, C, and D) was administered with 30 ml. of water at room temperature: antacid A, 22 ml., suspension; B, 22 ml., suspension; C, 5 ml., suspension; D, two tablets. Each antacid preparation contained aluminum and magnesium hydroxides; formulation C also contained magnesium carbonate and methyl polysiloxane.

The apparent onset and duration of gastric acid buffering activity following administration of the three liquid and one solid antacid formulations are reported in Table I.

Although all of the "improved" Heidelberg capsules were apparently operative, as determined by *in vitro* calibration in buffer solutions and recording of pH signal immediately after swallowing the device, in approximately 14% of the trials (5 of 35 experiments) the anticipated elevation of gastric pH after administration of antacid was not perceived. In 86% of the trials the onset of buffering activity (*i.e.*, elevation of gastric pH above 3.0) following administration of antacid was

[1] Medintron Corp. of America, New York, N. Y.

Table I—Onset and Duration (Time in Minutes) of Buffering Action following Administration of Gastric Antacid Preparations in Human Subjects as Recorded by Heidelberg Capsule Telemetry

Antacid A—Suspension			Antacid B—Suspension			Antacid C—Suspension			Antacid D—Tablet		
Subject	Onset[a]	Duration	Subject	Onset	Duration	Subject	Onset	Duration	Subject	Onset	Duration
1	1	2[d]	1	3	40	1	31	>16	1	2	>46
2	1	13[d]	3	5	24	5	1	12	12[b]	0	0
3[b]	0	0	5	9	8[d]	10[b]	0	0	13	1	6[d]
5	6	12[d]	6	1	11	11	37	>10	15	3	1[d]
6	7	>40	7	2	2[d]	12	2	>40	18	7	2[d]
7[c]	43	> 4	10	3	2[d]	14	7	28			
9	1	10[d]	11	7	8[d]	15[b]	0	0			
10	5	4[d]	12	1	22[d]	16	1	34			
11[b]	0	0				17	27	>20			
12	2	>46				18	25	>22			
13	4	4[d]				19	29	4			
Average onset	3.4(n=8)			3.9(n=8)			17.8(n=9)			3.3(n=4)	

[a] Gastric pH >3.0. [b] No response, subject not included in calculation of average value. [c] Atypical response, subject not included in calculation of average value. [d] Gastric pH nonrecordable after indicated time.

readily detectable. The apparent *in vivo* "failure rate" (14%) encountered in this study was, however, less than the approximately 50% "failure rate" found by other investigators (2) who examined capsules of an earlier design under essentially similar conditions (*i.e.*, unrestrained device in subjects sitting erect).

Considering the amount and composition of the antacid formulations used in this study, an initial rise in gastric pH following ingestion of any of the four preparations may be considered a predictable phenomenon. This applies also to those individuals who may have been subject to gastric hyperacidity at the time of antacid administration. That a pH rise was not detectable in some cases is consistent with the assumption of *in vivo* capsule failure. Transmitter failure in certain cases may have been attributable to location in the stomach, *i.e.*, the device may have lodged in an area of the mucosa whereby contact of the sensor with the gastric contents was prevented or impaired.

Evaluation of the data obtained in those cases where transmission of gastric pH values was confirmed suggests that the duration of the buffering action of antacids cannot be measured reliably by this technique. Approximately 40% of the capsules used in this investigation ceased normal transmission shortly after signaling onset of antacid-induced elevation of gastric pH. In view of the observed rapid increase in the gastric pH of fasted subjects to values which exceeded the capsule range (pH above 7), it is presumed that those capsules were emptied from the stomach together with the gastric contents. Emptying of the stomach is often accelerated by significant elevations in gastric pH (3). The capsule may be retained in the stomach for an arbitrary period by securing one end of a measured length of string to the capsule and the other end to the teeth after swallowing the transmitter. Since attachment of a restraining device would create an artificial situation in which the location of the capsule would be unrelated to retention of antacid in the stomach, it was not employed in this investigation.

The results of this investigation suggest that the *in vivo* performance of the modified Heidelberg telemetric capsule is not completely dependable. It may be considered a convenient and useful device for monitoring changes in gastric pH in the period immediately following administration of antacids whose buffering activity is qualitatively predictable. Duration of antacid-induced buffering effect could not, under the conditions of this study, be accurately ascertained, due possibly to acceleration of gastric emptying and consequent ejection of transmitter from the stomach.

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Formulation of a Morphine Implantation Pellet Suitable for Tolerance–Physical Dependence Studies in Mice

Keyphrases ☐ Morphine implantation pellet, formulation—tolerance, physical dependence studies ☐ Dependence studies—morphine pellet formulation ☐ Cellulose, microcrystalline—implantation pellets

Sir:

There is considerable current interest in the study of morphine addiction, tolerance, and physical dependence. When using laboratory animals (*e.g.*, mice) for such studies, an essential part of the procedure is