The Effect of Gastrointestinal Hormones on the Pertechnetate Imaging of Ectopic Gastric Mucosa in Experimental Meckel's Diverticulum

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Meckel's diverticula were simulated in 12 dogs by implanting vascularized patches of gastric wall onto Roux-en-Y loops of distal ileum. All animals had camera imaging studies every 10 min for 60 min, with computer acquisition (1-min frames) following intravenous injection of 2 mCi of pertechnetate. The scintigrams were repeated following (a) subcutaneous injection of pentagastrin (6 μg/kg) 15 min before injection of pertechnetate; (b) intravenous injection of glucagon (50 μg/kg) 10 min after the tracer injection; (c) pretreatment with pentagastrin plus glucagon as above; and (d) pretreatment with pentagastrin plus secretin (1 unit Boots/kg intravenously 10 min after the pertechnetate). Patches of ectopic gastric mucosa as small as 1 cm^2 were visualized. Pentagastrin alone accelerated accumulation of the tracer but resulted in a decrease in the target-to-background ratio. Glucagon alone enhanced late gastric mucosal activity by preventing washout of the intraluminal activity. The combination of pentagastrin and glucagon enhanced visualization and kept background activity lowest. These findings indicate a potential role for glucagon in the diagnosis of ectopic gastric mucosa in humans.

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Abdominal scintigraphy with pertechnetate (Tc-99m) for the detection of ectopic gastric mucosa (usually in Meckel's diverticulum) in the patient with rectal bleeding has been applied clinically for a decade. The superficial cells lining the surface of the gastric mucosa take up the intravenously injected pertechnetate anion [$^{99m}TcO_4^-$] and excrete it into the intestinal lumen, producing local accumulation of radioactivity that is visible on scintigram (*1*). A recent analysis of the reported clinical experience in 928 patients showed a sensitivity of 85% for the detection of surgically proven ectopic gastric mucosa.

False-negative studies may occur for several reasons: (a) the ectopic gastric mucosa may be too small, or it may not be secreting actively; (b) dilution (washout) of the intraluminal activity may occur by either hemorrhage or coexistent intestinal hypersecretion; (c) suboptimal scanning techniques overlapping normal abdominal organs and misinterpretation may prevent recognition of the abnormality (*1*). Experimental (*2–4*) and clinical (*5,6*) efforts to reduce the incidence of false-negative studies have met with variable success, and the mechanism of action of the various drugs claimed as effective has not been elucidated.

We studied the effect of the intestinal hormones pentagastrin, glucagon and secretin on the pertechnetate imaging of surgically simulated Meckel's diverticula in dogs. The results of visual and computer-assisted analysis are reported in this communication.

METHODS

Experimental model. Twelve adult mongrel dogs (weight 8–12 kg) had a preoperative pertechnetate study. Experimental Meckel's diverticula were then constructed by implanting a full-thickness vascularized patch of gastric wall onto the open end of a defunctionalized Roux-en-Y segment of distal ileum (Fig. 1). The surface areas of the transplanted patches varied from 1.1–4.5

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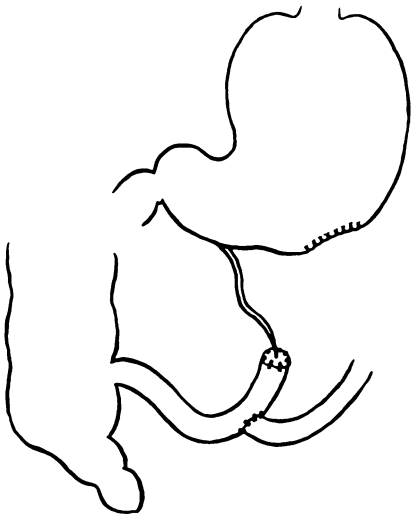

FIG. 1. Experimental preparation.

cm^2. A recovery period of 3 wk was allowed following this operation.

Radionuclide technique. In addition to the preoperative study, the animals underwent multiple postoperative pertechnetate scans. (a) Control (no hormones); (b) Pentagastrin (6 μg/kg ca. 15 min before injection of pertechnetate); (c) Glucagon (50 μg/kg i.v. 1 min after pertechnetate); (d) Pentagastrin and glucagon (time sequence as in (a) and (b)); (e) Pentagastrin and secretin (pentagastrin as in (b), secretin 1 unit Boots/kg i.v. 10 min after pertechnetate).

The control studies were performed 3–5 wk postoperatively; the others followed in a random order during a 2-mo period.

The animals were fasted for more than 8 hr before each examination. Pentobarbital (30 mg/kg i.v.) anesthesia was used. Potassium perchlorate was not administered, since it is known to affect adversely pertechnetate uptake by gastric mucosa (*7*). Two millicuries of sodium pertechnetate (Tc-99m) were injected intravenously and the dogs were imaged in the supine position with the regular-field-of-view, high-resolution detector of a gamma camera over the lower chest and abdomen. Polaroid scintigrams were obtained at 10-min intervals and data were stored in a minicomputer at 1-min intervals for 1 hr.

The images were evaluated by visual interpretation and by comparison with a phantom. This contained eight areas of activity (Tc-99m) in a background mimicking diffuse abdominal activity, with target-to-nontarget ratios (T/NT) varying from 2.5 to 200 as measured with the same camera system. Scores ranged from 0–4, as follows: zero for nonvisualization, half point for T/NT = 2.5, one for T/NT = 5, two for T/NT = 10, three for T/NT = 20, and four for T/NT > 50.

The computer-stored data were analyzed using time-activity curves for the regions of interest: stomach, duodenum, ectopic gastric mucosa, and background. The last included the right lower quadrant and the background of the entire abdomen, excluding gastric, duodenal, and ectopic gastric activity.

Changes in the activity within each of these areas were expressed as a percentage of the counts collected during the second 1-min period, except for the duodenum (same at 10 min), after tracer injection. To simplify the format, only the data at the end of each 10-min period up to 60 min will be presented.

RESULTS

General findings. In 11 of the 12 animals, the mucosa of the ectopic gastric patches was visualized on all of the radionuclide studies. The surface areas of the transplants measured at necropsy ranged from 1.0–3.2 cm^2, a consistent 20% decrease from the time of construction. One dog showed no evidence of focal right-lower-quadrant radioactivity on any of the studies, and at autopsy the transplant was found necrotic. No gastric mucosa was identified histologically.

Preoperative studies (Figs. 2a, 3a, 4a). The pertechnetate image of the abdomen of the normal dog differs from the human only in the location of the duodenal

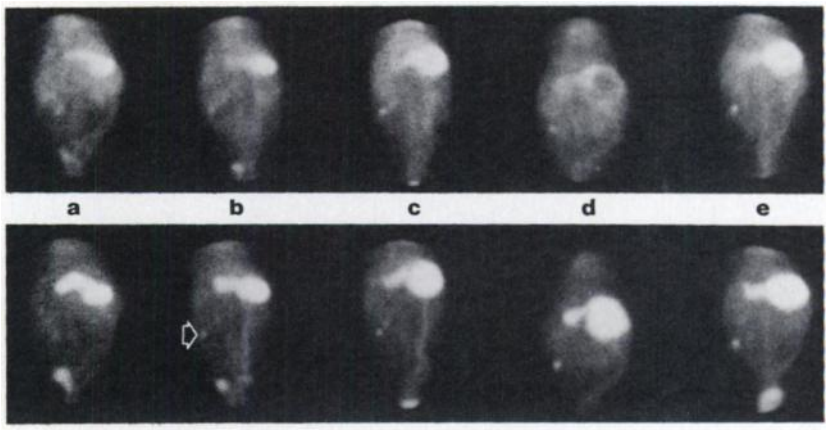

FIG. 2. Pertechnetate abdominal scintigrams of dog #3047 at 10 min (upper row) and 60 min (lower row) after injection. (a) Preoperative study; b–e, postoperative studies; (b) control (no hormones); (c) pentagastrin; (d) glucagon; (e) pentagastrin followed by glucagon.

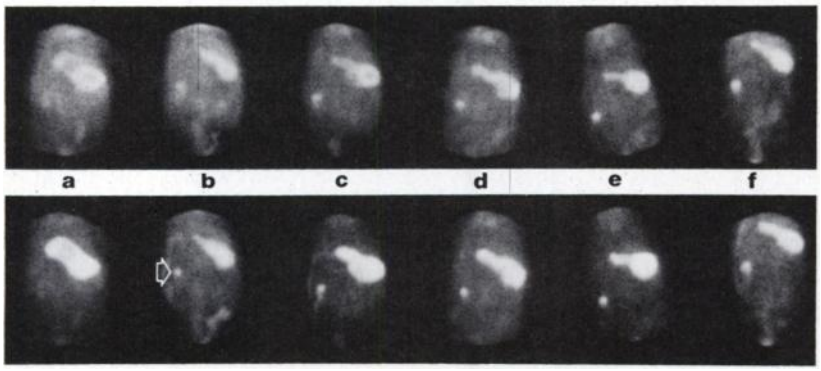

FIG. 3. Pertechnetate abdominal scintigrams of dog #3107 with a 3-cm² transplant at 10 min (upper row) and 60 min (lower row) after injection. (a) Preoperative study; b–f, postoperative studies; (b) control (no hormones); (c) pentagastrin; (d) glucagon; (e) pentagastrin followed by glucagon; (f) pentagastrin followed by secretin.

activity. The duodenum in the dog has a more lateral course and is visualized close to the right side of the abdomen, engulfing laterally the activity of the kidney. Otherwise, the abdomen shows the familiar picture of the negative "Meckel's scan" (*1*). It displays a nonhomogeneous distribution but without focal accumulation of activity, except for the normal blood pool of the abdominal vessels and organs. In the early pictures the stomach, kidneys, and large vessels are seen. The image of the stomach persists, with continuously increasing intensity; the images of the kidneys fade slowly; and those of the bladder, duodenum, and jejunum appear later.

Postoperative images. The ectopic gastric patches appeared as focal areas of hyperactivity in the right lower quadrant of the abdomen of each dog.

Control studies (*No hormonal pretreatment*) (*Figs. 2b, 3b, 4b*). The focus of accumulated activity within the transplant was visualized 10–20 min after the administration of the pertechnetate. The intensity of the activity generally increased subsequently but in some animals a falling off of the focus became apparent as technetium was washed away following the secretions. Often the duodenum was visualized in some images. In one dog, the control study showed the transplant better than after hormonal use.

Effect of pentagastrin (*Figs. 2c, 3c, 4c*). When pentagastrin was administered, the transplant became apparent earlier, reached peak intensity at 30–40 min, and occasionally faded later. The duodenum also visualized earlier, more consistently and intensely, and frequently resulted in perplexing images that obscured the location of the transplant. Washout of activity from the gastric patch was commonly observed.

Effect of glucagon (*Figs. 2d, 3d, 4d*). Although the ectopic gastric activity appeared as in the controls, glucagon administration produced a continuous increase of tracer intensity and often prevented visualization of the duodenum. In two dogs the glucagon effect lasted only 40–50 min.

Combined effect of pentagastrin and glucagon (*Figs. 2e, 3e, 4e*). Under the influence of both hormones the gastric patches visualized early (10 min), the intensity of their activity increased continuously, and they appeared more distinct than in the previous studies. No duodenal interference or washout was apparent.

Results of combined use of pentagastrin and secretin (*Figs. 3f, 4f*). Secretin produced no consistent effect upon the pentagastrin-induced results described above. The studies showed equal, better, or worse visualization of the transplants in comparison with pentagastrin alone.

Visual comparative analysis of the images. Using the images of the phantom and the grading method described earlier, the visual impressions of the patches in the different experiments are given in Table 1.

Computer analysis of the postoperative studies. The means of the unprocessed counts from different parts of the abdomen of the control and hormonal studies from eight dogs were calculated for 1–2 min and at 10-min intervals for 60 min after administration of pertechnetate (Table 2).

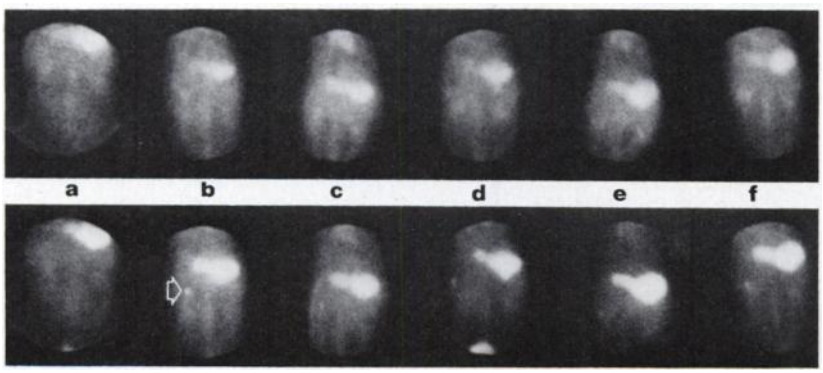

FIG. 4. Pertechnetate abdominal scintigrams of dog #3176 with a 1-cm² transplant at 10 min (upper row) and 60 min (lower row) after injection. (a) Preoperative study; b–f, postoperative studies; (b) control (no hormones); (c) pentagastrin; (d) glucagon; (e) pentagastrin followed by glucagon; (f) pentagastrin followed by secretin.

TABLE 1. SCORES* FOR DETECTABILITY OF ECTOPIC STOMACH AND OF THE DUODENUM (PARENTHESES)

Type of study	Min after pertechnetate injection						
	3	10	20	30	40	50	60
Control	1(0)	10(0)	16(2)	18(2)	22(3)	23(8)	24(9)
Pentagastrin	7(0)	16(2)	18(4)	21(8)	22(10)	21(13)	20(14)
Glucagon	3(0)	12(0)	19(0)	22(0)	22(3)	25(6)	23(4)
Pentagastrin and glucagon	7(0)	19(0)	21(0)	22(0)	25(1)	27(2)	28(3)

* Scoring system is described in text. Each number represents the sum of the scores for eight dogs.

Ectopic gastric activity (*Fig. 5*). The 1-2 min activity in the region where the transplant became apparent later gave the highest gross total counts in all studies, and although the transplants did visualize, the total counts of the area showed a continuous decrease. When the corresponding background activity was subtracted, the true accumulation was found (Fig. 5, Table 2). It is evident that glucagon sustained and increased the net activity of the gastric mucosal patches. These findings give numerical support to the visual analysis.

Duodenal activity (*Fig. 6*). The gross counts obtained over the duodenum were plotted as a percentage of the 10-min activity (the earliest time duodenum was seen). In the controls, duodenal activity initially remained low, paralleling the subsiding abdominal activity, but it increased at 1 hr as gastric emptying began. After pentagastrin alone, the activity in the duodenal area increased both absolutely and relative to the abdominal background. Glucagon alone, or even after pretreatment with pentagastrin, kept the duodenal activity at abdominal background levels.

DISCUSSION

Pertechnetate abdominal imaging to visualize ectopic gastric mucosa has a reported sensitivity of 85% (*1*). Nothing can be done to produce an anatomic advantage with regard to the size of the target tissue, and little to improve the position. It appears that increasing pertechnetate uptake within the gastric mucosa and reducing abdominal background activity should give improved results.

Pentagastrin has been shown to increase the gastric uptake of pertechnetate in experiments with in vitro counting of excised organs (*4*). Glucagon and secretin have been reported to be ineffective in these studies. We evaluated these hormones by visual and computer-assisted analysis of their effect on the pertechnetate uptake by transplanted gastric mucosa. This approach closely mimics human studies and evaluates the effect of these hormones both on the pertechnetate uptake of the transplant and on abdominal background. It directly addresses the question of whether hormonal pretreatment induces better visualization of the ectopic gastric

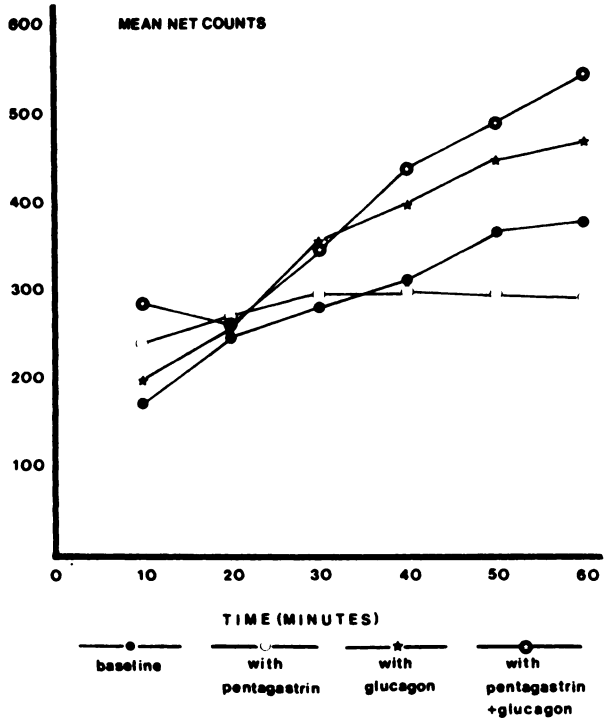

FIG. 5. Progress of net ectopic gastric activity; means of eight dogs (control and hormonal studies).

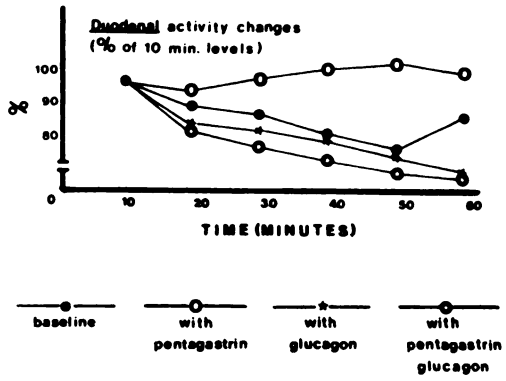

FIG. 6. Progress of duodenal activity from the 10-min levels in eight dogs (control and hormonal studies).

TABLE 2. COMPUTER ANALYSIS OF PERTECHNETATE REGION-OF-INTEREST DATA FROM EIGHT DOGS, WITH HORMONES INDICATED AND WITHOUT (BASE-LINE)

Abdominal background counts (excluding stomach, duodenum, and transplant) at times indicated: mean ± s.d., with (percentage of 1-min count)

Min	Baseline	Pentagastrin	Glucagon	Pent. and glucag.
1	81 ± 17(100%)	77 ± 15(100%)	74 ± 14(100%)	76 ± 14(100%)
10	73 ± 14(91%)	68 ± 13(88%)	65 ± 12(88%)	65 ± 11(86%)
20	68 ± 13(84%)	62 ± 11(81%)	62 ± 11(84%)	60 ± 10(79%)
30	64 ± 12(80%)	59 ± 10(77%)	56 ± 10(76%)	56 ± 9(74%)
40	60 ± 11(75%)	57 ± 9(74%)	53 ± 10(72%)	52 ± 8(68%)
50	58 ± 11(71%)	55 ± 8(71%)	51 ± 11(69%)	48 ± 7(63%)
60	57 ± 11(71%)	54 ± 7(70%)	50 ± 12(68%)	46 ± 7(61%)

Gross counts in stomach ROI, mean ± s.d., with (percentage increase over 1-min level).

Min	Baseline	Pentagastrin	Glucagon	Pent. and glucag.
1	14802 ± 1899(0%)	16121 ± 4290 (0%)	17325 ± 3712 (0%)	18240 ± 2924 (0%)
10	17541 ± 3050(19%)	20831 ± 6811 (29%)	20368 ± 6834 (18%)	23272 ± 6061 (28%)
20	20481 ± 4547(38%)	25428 ± 9953 (58%)	27904 ± 8893 (63%)	30112 ± 8795 (65%)
30	22705 ± 5774(53%)	27650 ± 10067(72%)	32242 ± 8279 (86%)	34743 ± 10381(90%)
40	25385 ± 7479(71%)	29918 ± 11314(86%)	35088 ± 9187 (103%)	38720 ± 11597(112%)
50	27043 ± 7855(83%)	31647 ± 11920(96%)	37022 ± 9828 (114%)	41508 ± 11862(128%)
60	27355 ± 6343(85%)	32347 ± 13237(101%)	38115 ± 11115(120%)	43450 ± 12373(138%)

Gross counts in duodenal ROI, mean ± s.d., with (percentage of count at 10 min)

Min	Baseline	Pentagastrin	Glucagon	Pent. and glucag.
1	4830 ± 1983	5470 ± 1732	3307 ± 1301	3503 ± 657
10	3637 ± 1377(100%)	3970 ± 1229(100%)	2466 ± 870 (100%)	2514 ± 512 (100%)
20	3365 ± 1328(93%)	3849 ± 1308(97%)	2160 ± 807 (88%)	2215 ± 458 (88%)
30	3320 ± 1607(91%)	4018 ± 1520(101%)	2115 ± 847 (86%)	2044 ± 432 (81%)
40	3075 ± 1337(85%)	4101 ± 1707(103%)	2035 ± 1007(83%)	1937 ± 475 (77%)
50	2924 ± 1302(80%)	4219 ± 1708(106%)	1982 ± 792 (80%)	1844 ± 528 (73%)
60	3261 ± 1975(90%)	4089 ± 1582(103%)	1821 ± 613 (74%)	1804 ± 513 (72%)

Mean Activity in the Ectopic Gastric Mucosa

Min	Baseline		Pentagastrin		Glucagon		Pent. and glucag.	
1	1757 ± 742		1611 ± 524		1756 ± 750		1608 ± 512	
10	1554 ± 565	178 ± 255	1451 ± 431	247 ± 237	1555 ± 572	206 ± 304	1461 ± 421	287 ± 346
20	1514 ± 524	252 ± 293	1374 ± 429	275 ± 272	1563 ± 621	269 ± 326	1342 ± 428	268 ± 325
30	1483 ± 551	286 ± 340	1353 ± 403	300 ± 273	1546 ± 522	359 ± 418	1319 ± 398	359 ± 461
40	1470 ± 498	319 ± 320	1336 ± 408	303 ± 264	1541 ± 514	402 ± 428	1348 ± 399	441 ± 434
50	1456 ± 495	370 ± 368	1343 ± 353	299 ± 285	1552 ± 508	453 ± 452	1340 ± 415	490 ± 435
60	1528 ± 531	380 ± 362	1306 ± 350	295 ± 254	1543 ± 551	473 ± 521	1362 ± 385	549 ± 461

* Mean gross counts ± s.d.

† Mean net counts ± s.d.

mucosa. It was not technically feasible to produce ectopic patches smaller than 1 cm^2. The smallest transplants we constructed were visualized on the control scans. We did not achieve the ultimate model of a patch that would not visualize on the control study, becoming visible after hormonal treatment. Thus, the results of this study were quantitative rather than qualitative. We found that, compared with controls, pentagastrin increases the pertechnetate uptake by the gastric mucosa, as others have found previously (*3,4*). However, because of washout of the intraluminal activity and a concomitant increase in background, the gastric patches did not

visualize better in most of the animals studied.

Addition of glucagon enhanced the effect of pentagastrin by preventing the latter hormone's untoward effects. Glucagon alone gave better results than control or pentagastrin alone; it increases T/NT ratio by preventing washout and relative background enhancement, which happens after pentagastrin and, to some extent, in the pertechnetate studies of the untreated controls.

Pentagastrin probably exerts a direct effect on the mucosa. It has been shown that this hormone increases the secretory activity of the intestine (*8*). Glucagon may exert its action (a) by preventing washout of the intraluminal activity excreted locally by the transplant, and (b) by preventing the discharge of stomach activity into the small bowel. It is known that glucagon inhibits gastrointestinal motility (*9,10*). It has also been reported that H_2 receptor blockage with cimetidine may have a similar effect on imaging by blocking the release of pertechnetate into the lumen of the intestine (*11*).

It appears reasonable to evaluate the effectiveness of glucagon alone or the combination of pentagastrin and glucagon in the visualization of suspected ectopic gastric mucosa in patients with Meckel's diverticulum.

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