The usefulness of a tracer agent as a routine radiopharmaceutical is determined not only by its in vivo behavior but also by practical aspects such as ease of preparation and stability. In this regard, ^{99m}Tc-L,L-EC is preferable to ^{99m}Tc-MAG3 even though the preparation of both radiopharmaceuticals is a two-step procedure. Technetium-99m-L,L-EC has the convenience of a labeling procedure that can be performed rapidly at room temperature to achieve a preparation of high radiochemical purity that remains stable throughout the day (*11*). By contrast, the preparation of ^{99m}Tc-MAG3 involves a boiling step and stability after this step is limited to between 1 and 4 hr depending on the concentration of the preparation.

CONCLUSION

In our series of patients with chronic renal failure, ^{99m}Tc-L,L-EC compared favorably with ^{99m}Tc-MAG3. Technetium-99m-L,L-EC is an attractive alternative to ^{99m}Tc-MAG3 in patients with impaired renal function. It provides equally high-quality images but has the advantage of enhanced simplicity of preparation. Furthermore, compared to ^{99m}Tc-MAG3, it more closely resembles hippuran.

ACKNOWLEDGMENTS

We thank Prof. A.M. Peters, Department of Radiology, Hammersmith Hospital, for his advice during the preparation of this manuscript. We are grateful to Dr. D. Thompson and Prof. G. Neild for their cooperation and the selection of the patients.

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Evidence of Accelerated Gastric Emptying in Longstanding Diabetic Patients After Ingestion of a Semisolid Meal

Rainer W. Lipp, Wolfgang J. Schnedl, Heinz F. Hammer, Peter Kotanko, Georg Leb and Guenter J. Krejs

Divisions of Nuclear Medicine, Diabetology and Gastroenterology, Departments of Internal Medicine, Karl-Franzens-University, Graz; and Barmherzigen Brüder Hospital, Graz, Austria

This study investigated the prevalence of accelerated gastric emptying in 40 consecutive nonselected patients with longstanding insulin-dependent diabetes mellitus (range 11–54 yr; mean 27 yr). **Methods:** The gastric emptying of a semisolid meal labeled with ^{99m}Tc was continuously recorded with a dual-head gamma camera for 90 min in patients who were supine. **Results:** Eleven patients demonstrated delayed gastric emptying, but three male diabetics showed accelerated gastric emptying with retention values that were different from controls already after 10 min of recording (89% ± 3% versus 96% ± 4%; $p < 0.02$). During the 90-min segment, accelerated gastric emptying reduced initial gastric contents to 11% ± 8% ($p < 0.001$) as compared to 50% ± 10% in control subjects and 78% ± 6% ($p < 0.001$) in patients with delayed gastric emptyings. Accelerated gastric emptying was characterized by an almost equal initial meal distribution in proximal and distal compartments of stomach, both emptying approximately 90% of their contents within 90 min. Normal and delayed gastric emptying was characterized by a 60%–40% initial ratio of meal distribution between gastric compartments. During normal emptying, both compartments reduced contents with approximately 50%, but delayed gastric emptying was caused by only a 15% reduction of proximal contents accompanied by a 34% reduction in distal contents. **Conclusion:** Recording in the supine position to abolish gravitational influences demonstrated accelerated gastric emptying of a firm semisolid meal with a prevalence of 8%. However, delayed gastric emptying was shown as the predominant gastric manifestation of longstanding insulin-dependent diabetes mellitus with a prevalence of 28%.

Key Words: accelerated gastric emptying; insulin-dependent diabetes mellitus; supine position; semisolid test meal

J Nucl Med 1997; 38:814–818

Received Mar. 21, 1996; revision accepted Sep. 11, 1996.

For correspondence or reprints contact: Rainer W. Lipp, MD, Division of Nuclear Medicine, Dept. of Internal Medicine, Auenbruggerplatz 15, A-8036 Graz, Austria.

Delayed gastric emptying is well-documented in patients presenting insulin-dependent diabetes mellitus (IDDM) with a prevalence up to 58% (*1–5*). Accelerated gastric emptying is frequently described in patients after gastric surgery but there are only a few reports of rapid emptying in patients with diabetes mellitus (*6–8*). Three studies reported a prevalence for accelerated emptying of 100% and another one of 13% in early noninsulin dependent diabetes mellitus (*9–12*). One study of 45 patients with longstanding IDDM (*1*) reported accelerated emptying of the liquid phase in two patients and of the solid phase in one patient (*1*). Mecklenbeck et al. (*13*) reported accelerated gastric emptying of only the solid phase in six of 22 patients. A recent article reported accelerated emptying of a solid meal in eight of 21 patients (*14*). This ambiguity in results suggested a prospective investigation of accelerated gastric emptying after ingestion of a firm semi-solid meal that combines the emptying characteristics of liquid and solid meals.

MATERIALS AND METHODS

Patients

This study included 40 nonselected consecutive patients (15 men, 25 women, age range 22–69 yr; mean 46 yr) with a body mass index (BMI) of 23.5 ± 3.3 kg/m^2 who were being followed for longstanding IDDM in the outpatient clinics of the Department of Internal Medicine, Karl-Franzens-University and the Barmherzige Brüder Hospital in Graz, Austria. The mean duration of diabetes was 27 yr (age range 11–54 yr). Results were compared with data obtained from 20 healthy volunteers (12 men, 8 women; age range 26–61 yr; mean 39 yr), BMI of 22.2 ± 3.1 kg/m^2. All patients and volunteers were free of medication known to influence gastrointestinal motility and none had a history of gastrointestinal surgery except for appendectomy.

Assessment of Gastric Emptying

Preparation of the test meal: 60 g instant potato flakes containing dry milk were stirred gently in 250 ml boiling tap water until ready. Before consumption, 200 g mashed potatoes were thoroughly mixed with 0.5 g Dowex 2 × 8 beads (diameter 0.83–0.3 mm) previously labeled with 37 MBq (1 mCi) ^{99m}Tc. The meal was ingested while still warm within 5–7 min. Its ingestion was concluded by an oral rinse with 100 ml tap water, bringing the total weight of the test meal to 300 g (*15*). The meal contained 3.8 g protein, 1.6 g fat and 21 g carbohydrate representing 480 kJ (120 kcal).

Binding Efficiency of Dowex 2 × 8 Beads in Natural Gastric Juice

After labeling with 37 MBq ^{99m}Tc, 0.5 g Dowex 2 × 8 beads were placed in 10-ml natural gastric juice at 37°C and gently stirred for 90 min. The gastric juice was obtained from five patients during gastroscopy with normal endoscopy. Radioactivity bound to beads was measured after separation of beads from gastric juice by filtration. Free radioactivities in gastric juice and in filter paper were compared.

Protocol

Patients were asked to abstain from tobacco and alcohol for 24 hr before scintigraphy, fast overnight and include the carbohydrates of the test meal in the dietary regimen of the next day. Blood glucose levels were determined immediately before ingestion of the test meal. All patients presented glucose levels between 5.6 and 10.0 mmol/liter before scintigraphy. All tests began at approximately 9:00 am. Data acquisition in the supine position started 10 min after commencement of meal ingestion and continued for a period of 90 min.

Recording

Imaging was performed using a dual-head gamma camera equipped with low-energy, high-resolution, parallel-hole collimator systems and interfaced to a computer. Simultaneous anterior-posterior and posterior-anterior 15-sec exposures were continuously recorded with a matrix of 64 × 64 (photo peak 140 kev, window setting 10%).

Data Processing and Analysis

A time-lapse cine playback was created to view gastric emptying dynamically and to facilitate identification of regions of interest (ROIs). Mirror framed ROIs, tightly encompassing the whole gastric area, were manually delineated and the results stored. Emptying curves expressed as percentage retention of isotope versus time were Chebyshev fitted for display (*16*). For data analysis, decay-corrected percent retention values were computed as the algebraic means of three temporarily subsequent ROIs for instance at 0, 30, 60 and 90 min, this is to say that algebraic means were computed from the values at time 0, 0 + 15 sec and 0 + 30 sec then at time 15 min − 15 sec, at time 15 min and at 15 min + 15 sec and so on. Geometric means of corresponding algebraic means (anterior, posterior views) were calculated to compensate for the gamma attenuation due to depth differences of the contents during gastric passage (*17*). Results of patients that were outside the mean retention values ± 2 s.d. obtained in control subjects indicated either delayed or accelerated gastric emptying. Half-hour slope values of retention time diagrams were computed at time 0, 30 and 60 min.

Calculation of Retention Values Within Proximal and Distal Stomach Compartment

The gastric ROI was divided in two equal areas by using the cursor facility of the computer to place a line across the stomach so that 50% of pixels indicating gastric contents were present in each area, irrespective of the number of isotope counts in each pixel (*18*). The two areas were designated as proximal and distal compartment. The total counts (decay corrected geometric means) in the three regions (total stomach, proximal and distal compartment) were then calculated at time 0 and every tenth minute thereafter. The radioactivity in each region at any time point was expressed as a percentage of initial radioactivity.

Statistical Analysis

Student's unpaired Student's t-test was used as applicable. Results are shown as mean ± s.d. A p value of <0.05 was considered as significant in all analyses.

RESULTS

Three male patients (8%) of 40 longstanding insulin-dependent diabetics showed accelerated gastric emptying of the semisolid meal. Eleven patients (28%) demonstrated delayed emptying and the rates of the remaining 26 patients (64%) fell within the range of control subjects. Figure 1 shows individually the three accelerated emptying curves and, for comparison, the range of normal emptying and the mean curve of delayed emptying. All three curves of accelerated emptying commenced without lag periods and fell below the range of controls after only 10 min (89% ± 3% versus 96 ± 4; $p < 0.02$). The curve of one patient entered the range of control subjects between 12 and 42 min and descended thereafter steeply to final gastric contents of 5% after 90 min. The emptying curve of another patient descended almost linearly to final contents of 20% and that of the third patient presented the monoexponential type of emptying with a final meal residue of 7%. Accelerated gastric emptying reduced gastric contents to final retention value of 11% ± 8% ($p < 0.001$) as compared to 50% ± 10% in control subjects and 78% ± 6% in patients with delayed gastric

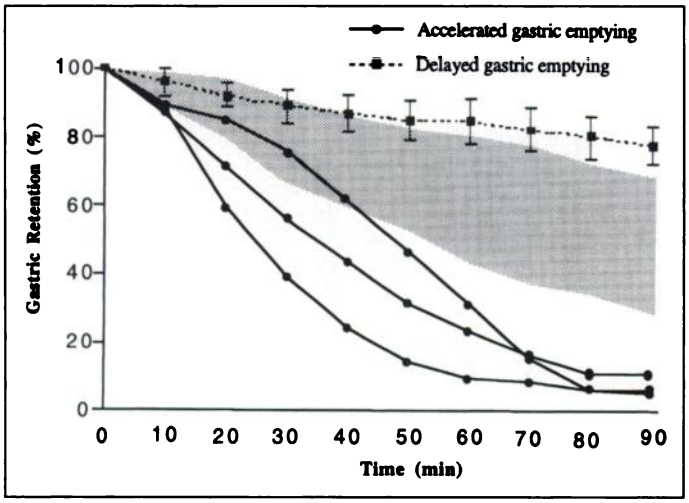

FIGURE 1. Time retention diagrams. Accelerated gastric emptying = individual emptying curves for three patients. Delayed gastric emptying = mean ± s.d. of 11 patients. Shaded area = gastric emptying of 20 controls (mean ± 2 s.d.).

emptying ($p < 0.001$). In accelerated gastric emptying, the mean slope value of the emptying curves were significantly larger until 60 min than that in control subjects as indicated by the respective values of 1.6 ± 0.4 versus 0.7 ± 0.2 ($p < 0.01$; 0–30 min), 1.1 ± 0.2 versus 0.6 ± 0.3 ($p < 0.01$; 30–60 min) and 0.3 ± 0.3 versus 0.5 ± 0.4 (ns, 60–90 min).

Differences in the rate of gastric emptying were accompanied by distinctly different meal distribution patterns within the proximal and the distal compartment of stomach. Accelerated gastric emptying was characterized by almost equal initial mean retention values of 47% in the proximal and 53% in the distal compartment (Fig. 2A). This ratio was only little affected during the recording time. The final retention values were 6% in the proximal and 5% in the distal compartment. Patients with gastric emptying within the range of control subjects demonstrated an initial ratio of gastric contents of 58% in the proximal and 42% in the distal compartment (Fig. 2B). At the end of recording the proximal compartment contained 31% and the distal compartment contained 21% of the meal. Patients with delayed gastric emptying demonstrated an initial meal distribution of 62% (proximal compartment) and 38% (distal compartment), which changed to 53% and 25%, respectively (Fig. 2C).

These differences were not caused by dissociation of the radiolable from the Dowex 2 × 8 beads. The resin lost only 1.8% ± 0.1% of the originally bound radioactivity during 90 min in natural gastric juice.

Accelerated emptying was demonstrated relatively late in the course of diabetes, namely 29, 30 and 46 yr after onset of disease. In comparison, delayed gastric emptying was demonstrated already after 11 yr, the latest after 54 yr of diabetes. There were no statistical differences in HbA1c values in patients with accelerated (7.9% ± 0.7%), normal (8.7% ± 1.6%) and delayed gastric emptying (8.7% ± 1.7%).

DISCUSSION

Our investigation of 40 nonselected consecutive patients presenting with IDDM revealed accelerated gastric emptying of a semisolid meal in the supine position with a prevalence of 8%.

The time-retention diagrams of patients with accelerated emptying differed after only 10 min from control subjects, and showed interindividual differences in slope characteristics. In one patient, the emptying was fast during the first 12 min, slowed a little until 42 min and accelerated again thereafter. The second patient had a linear type of emptying. Both, therefore,

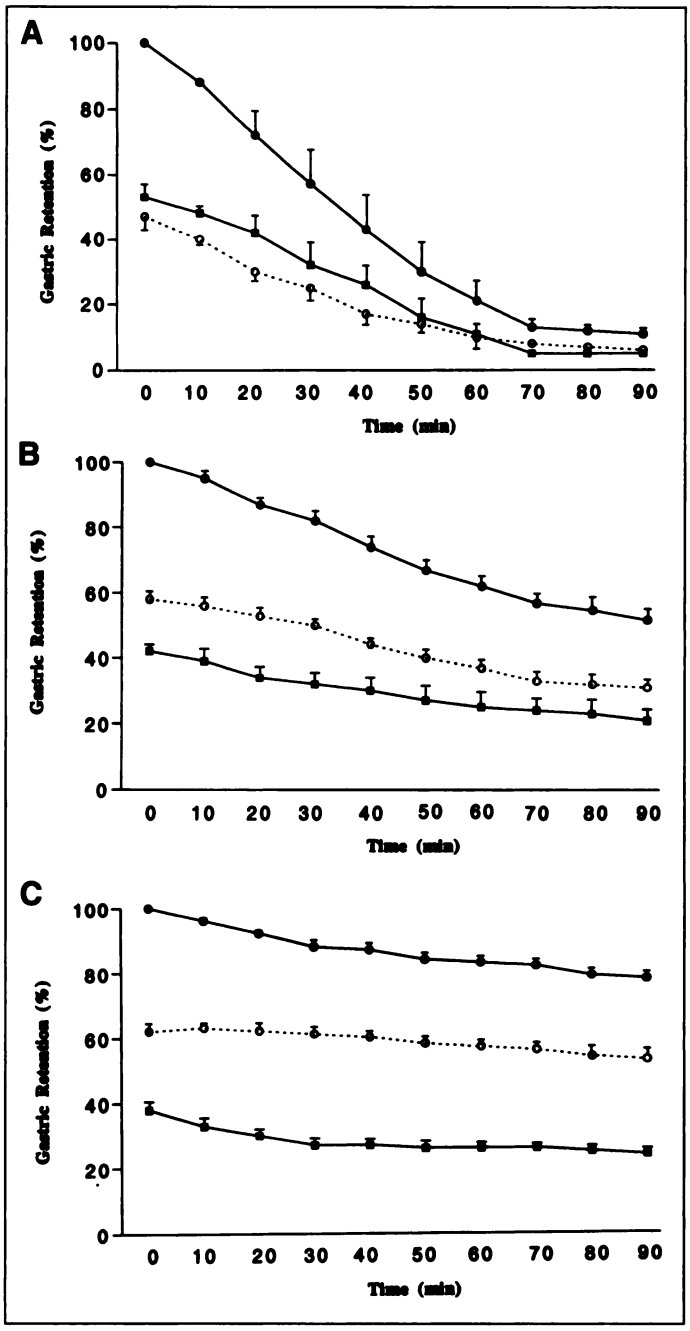

FIGURE 2. Time retention diagrams show distribution of test meal in proximal and distal gastric compartments. (A) Accelerated gastric emptying (n = 3). (B) Normal rate of emptying (n = 11). (C) Delayed gastric emptying (n = 11). Closed circles = total gastric contents; open circles with dotted lines = proximal compartment; squares = distal compartment. Data points show group mean (s.e.m.).

resembled the emptying pattern of a solid meal. The third patient emptied the meal almost monoexponentially, mimicking the pattern of a liquid meal. Thus, the curve profiles reflect the rate of gastric emptying becoming rather exponential with the increase of emptying dynamics. These differences were revealed by continuous imaging resulting in 720 exposures per patient. Seven temporarily spaced recordings (every 15th min) would necessitate curve fittings likely to obscure the real emptying profile depending on the fitting procedure used (*19,20*). Sole determinations of gastric half-emptying times may also be misleading in case of emptying rates changing with time. The semisolid meal of firm consistency used in this study was prepared to constant physical and chemical composition to avoid variations in emptying characteristics likely to occur

in meals of complex composition (*21*). Thus, the curve profiles of rapid emptying reflect the capacity of this meal to combine the emptying characteristics of liquids and solids.

Rapid gastric emptying was not mimicked by dissociation of the radiolabel from the Dowex 2 × 8 beads. The resin lost only 1.8% ± 0.1% of the originally bound radioactivity during 90 min in natural gastric juice. Earlier in vitro tests demonstrated that mashed potatoes prepared to firm consistency withstand liquefaction by natural or artificial gastric juice for at least 5 hr (*15*). Furthermore, accelerated emptying was not caused by meal liquefaction since it commenced without apparent lag periods providing the necessary time for liquefaction. Unlike solid meals, the gastric emptying of semisolid meals is not affected by differences in masticatory efficiency (*22*). In addition, the use of a monophasic semisolid meal facilitates the correct interpretation of results because there is no need to correct scattering caused by Compton effects of doubly labeled biphasic meals (*23*).

The control group of healthy volunteers had relatively more men than the patient group. This seems to be acceptable since all patients with accelerated gastric emptying were men who were not influenced by changes in sexual hormone levels (*24*). The three patients demonstrated rapid gastric emptying relatively late, namely 29, 30 and 46 yr after onset of diabetes, possibly as a consequence of prolonged duration. In comparison, accelerated emptying has been demonstrated already 2–4 yr after onset of noninsulin-dependent diabetes and has been discussed as precondition for the development of this type of diabetes (*9–11*).

Appropriate gastric emptying depends on the balance between propulsive forces such as fundic tone, antral contractility and antroduodenal coordination and restraining forces such as pyloric contraction, and impaired intestinal motility (*25*). A disturbed interplay of these forces is reflected by different distribution patterns of contents within gastric compartments.

Accelerated gastric emptying of a semisolid meal in the supine position was characterized by an almost equal filling of both gastric compartments. The proximal compartment moved its contents with a similar rate to the distal compartment as the latter emptied its contents into the duodenum. Both reduced their contents by approximately 90% during 90 min. In contrast, delayed as well as normal gastric emptying was characterized by an initial higher grade of filling of the proximal compartment with a ratio of approximately 60%–40%. In normal emptying, the proximal compartment reduced its contents by 47% and the distal compartment by 50%. In delayed gastric emptying, the proximal compartment emptied only 15% of its contents and the distal compartment 34%, resulting in a relative meal distribution of 68% in the proximal and 32% in the distal compartment after 90 min. This indicates a more inhibited propulsive function of the proximal gastric compartment in comparison to patients with normal emptying.

In the supine position, the antrum of a stomach containing the used test meal is situated some 40 mm above the level of fundus. This was shown by three-dimensional reconstruction of gastric contents based on SPECT images of eight healthy volunteers after ingestion of the semisolid meal (*26*). Whereas in the sitting, semireclining or upright position gravity may support gastric emptying. The accelerating effect is, therefore, abolished or at least negligible in the supine position. An adequate pressure gradient has to be generated by the stomach to empty a liquid against gravity surmounting the level difference. Even more propulsive force should be necessary to propel a firm semisolid meal from the antrum to pylorus, pyloric resistance notwithstanding. A recent study investigated gastric emptying of a biphasic meal in patients with asymptomatic noninsulin-dependent diabetes mellitus. The authors demonstrated normal emptying of the solid phase but significantly accelerated emptying of the liquid phase which they explained by greater phasic contractions of the proximal stomach (*10*). The design of our study does not allow a direct conclusion concerning the mechanism underlying nonsurgical dumping in the supine position which may differ in respect to development and course of diabetes. Mechanisms similar to those suggested to be responsible for dumping after gastric surgery, like increased phasic or tonic contractile activity, decreased accommodation of the proximal stomach or decreased resistance at the gastroduodenal junction may also play a role in patients without prior surgery (*27*). Additional manometric and electrophysiologic studies will be necessary to further characterize the underlying mechanisms causing accelerated gastric emptying in patients with long-standing IDDM.

CONCLUSION

Continuous imaging after ingestion of a semisolid meal, prepared to constant physical and chemical consistency proved to be advantageous to demonstrate reliably changes in gastric emptying rates. This method demonstrated accelerated gastric emptying as a late secondary manifestation of longstanding IDDM with a prevalence of 8%. Accelerated gastric emptying was distinguished from normal and delayed emptying by differences in time-retention diagrams, initial meal distribution between proximal and distal compartments of stomach and their different emptying rates. Presuming that gastric steric configuration investigated in control subjects is not altered by diabetes, in the supine position, gastric contents has to be lifted against gravity to be propelled from the antrum to the pylorus. Delayed gastric emptying remains, with a prevalence of 28% and is the more common disturbance of gastric emptying in patients with longstanding IDDM.

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Disseminated Islands of Gastric Mucosa in Jejunum and Ileum Detected by Technetium-99m-Pertechnetate Scintigraphy

Volker M. Heinrichs, Markus J. Kemper, Martin Burdelski, Dietrich Kluth, Dirk E. Mueller-Wiefel, Hansjoerg Schaefer and Martin Luebeck

Division of Nuclear Medicine, Departments of Pediatrics, Pediatric Surgery and Department of Pathology, University Hospital Eppendorf, Hamburg, Germany

Disseminated islands of gastric mucosa are very rare in the small intestine. The secretion of hydrochloric acid can lead to ulceration which results in gastrointestinal bleeding. It is often difficult to localize the focus in case of gastrointestinal blood loss especially in the small bowel. Technetium-99m-pertechnetate scintigraphy may be a helpful tool in detecting ectopic gastric mucosa. We report a case of a 21-mo-old boy with recurrent gastrointestinal bleeding. By using pertechnetate scintigraphy, extensive tracer accumulation in the jejunum and proximal ileum was detected. Histologically, multiple islands of ectopic gastric mucosa were found in about 50 excited mucosal and transmural biopsies. The unusual finding of disseminated accumulation of ^{99m}Tc-pertechnetate in the small intestine was the diagnostic clue for such a rare disease.

Key Words: ectopic gastric mucosa; technetium-99m-pertechnetate; gastrointestinal bleeding

J Nucl Med 1997; 38:818–820

Endoscopy and radiograph studies are able to locate most of the bleeding sources in patients with gastrointestinal blood loss. These methods, however, are unsuccessful in about 10% of patients with acute or chronic bleeding (*1,2*). In most of these cases, there are lesions in the small bowel which are difficult to localize. Mostly hemorrhage in childhood is caused by ectopic gastric mucosa in Meckel's diverticulum which results in peptic ulceration (*3*). Technetium-99m-pertechnetate scinitigraphy can be extremely helpful in detecting ectopic gastric mucosa as possible source of hemorrhage.

In this case report, we present a 21-mo-old boy with recurrent gastrointestinal bleeding. The pertechnetate scintigraphy performed to rule out Meckel's diverticulum showed extensive tracer accumulation throughout the jejunum and proximal ileum, which histologically disclosed as disseminated islands of gastric mucosa in the small bowel.

Received May 10, 1996; accepted Oct. 2, 1996.

For correspondence or reprints contact: Volker Heinrichs, MD, Department of Radiology, University Hospital Eppendorf, Martinstrasse, 52, 20246 Hamburg, Germany.

CASE REPORT

A 21-mo-old boy with known chronic renal failure, caused by dysplastic solitary kidney, was admitted to our hospital with a history of rectal bleeding. During the past 3 mo there was a continuous moderate decrease in serum hemoglobin, which was interpreted as developing renal anemia. Before admittance, the child's mother reported on occurrence of bloody stools and melaena. The result of the physical examination was inconspicuous except for a moderate pallor. Hemoglobin on admittance was 5,1 g/dl, hematocrit 16%, WBC 17,3/nl and CRP $<$ 10 mg/l.

Endoscopy of the stomach and colon did not reveal a bleeding site. To rule out a bleeding Meckel's diverticulum a ^{99m}Tc-pertechnetate scan was performed several days later using a gamma camera equipped with a LEHR collimator. After injection of 50 MBq ^{99m}Tc-pertechnetate, we first acquired a dynamic study over 5 min. Then static images of each 600,000 counts were taken every 10 min up to 4.4 hr p.i. There was a hyperperfusion in the upper abdomen followed by a tracer accumulation throughout the entire jejunum and proximal ileum beginning at the flexure of Treitz, which increased with time and paralleled the activity of the gastric mucosa (Fig. 1). Maximum intensity was reached 10 min p.i. and then constantly persisted. There was no transport within the small bowel during the investigation. Meanwhile, there was an increase of CRP to 84 mg/l so we first suggested unspecific tracer uptake in inflammatory small bowel disease.

Under antibiotic treatment with ampicillin and sulbactam (Unacid®), rectal bleeding ceased for 1 wk in accordance with stable hemoglobin and hematocrit. A control scintigraphy performed 3 wk later showed an unchanged state, thus, inflammation was excluded.

We finally suggested that disseminated gastric mucosa in the small bowel must have been responsible for the extensive tracer accumulation. After the scintigraphy, the patient developed abdominal pain. Since sonographically an intussusception was suspected, the patient underwent emergency laparotomy. Intraoperative inspection of the small intestine revealed multiple ill-defined tissue islands on the serosa site of the jejunum and proximal ileum. One