Glucagon is administered at the same time as a barium meal in order to facilitate X-ray examination of various intestinal organs.

1 Claim, No Drawings
GLUCAGON AS A DIAGNOSTIC AID IN GASTROINTESTINAL RADIOLOGY

BACKGROUND OF INVENTION

Physicians have been examining intestinal organs by X-ray and fluoroscopy for many years with the aid of various X-ray visualization media, the choice of media depending on the organ to be visualized. In order to facilitate visualization of the gastrointestinal tract, medication may be given to relax or contract the organ for better visualization or delineation of pathologic conditions. For example, in hypotonic duodenography, the duodenum is intubated under fluoroscopic control allowing for the direct introduction first of barium (as part of a barium meal) and then air into the duodenum. A barium air contrast study of the duodenum can be thus obtained. An anticholinergic drug is customarily administered parenterally to the patient being examined to induce duodenal hypotonicity for the better visualization of this organ. Anticholinergic drugs which have been used include atropine, propantheline bromide, and other similar drugs. Unfortunately, because of the large doses that need to be used to produce the desired effect, the anticholinergic drugs are accompanied by the classical side effects common to these agents. These side effects include urinary hesitancy and retention, dryness of the mouth and throat, nasal pharyngeal irritation, blurring of near vision, tachycardia, headache, and general malaise. With X-ray radiography of other organs such as the stomach, small bowel, and colon, it has also been customary to use an agent which would relax the organ during the procedure.

Glucagon is a hormone which has been stated to inhibit gastrointestinal motility in human subjects according to Foa and Galansino, *Chemistry and function in Health and Disease* (Charles C. Thomas, Springfield, Ill. 1962) and to Lawrence: *Medical Clinics of North America* 54:183–190, 1970. Its relaxing effect on the gallbladder during X-ray radiography has been described by Chernish, et al: *Gastroenterology* 62:1218, June 1972, and its effect in hypotonic duodenography was published in *Gastroenterology* 63:392, September 1972. It is an object of this invention to provide a method for conducting X-ray radiography and fluoroscopy of various intestinal organs in which a relaxant free from undesirable side effects is used in conjunction with an X-ray visualization medium in order to obtain better visualization of the gastrointestinal tract.

SUMMARY OF THIS INVENTION

This invention provides a process for improving the visualization of the intestinal tract by the use of X-ray radiography and fluoroscopy which comprises administering to the patient glucagon in addition to an X-ray visualization medium prior to radiographic examination. The intestinal organs which can be better visualized by the concurrent use of glucagon and an X-ray visualization medium according to the process of this invention include the stomach, duodenal cap, duodenal loop, small bowel, and the colon. For a visualization of the stomach, duodenum, and small bowel the X-ray visualization medium is a barium meal. For colon studies, a barium enema is given.

A particularly valuable use of the process of this invention is in connection with hypotonic duodenography. The use of glucagon as a relaxant of the intestinal tract in this radiographic procedure is illustrated by the following example.

In a double-blind study, 12 healthy males ranging in age from 21 to 31 years were given either 2 ml of normal saline or 2 mg of glucagon intravenously. Drugs were coded numerically in consecutive order so that the radiologist had no indication of the medication that was given. On the day of the test, after a light liquid breakfast, no other fluids or smoking was allowed. In the early afternoon, each subject was given ½ to 1 cup of a barium meal and the duodenum was observed fluoroscopically. Medication was then administered (either saline or glucagon) by the intravenous route and the duodenum in each subject was observed for short periods at 1–2 minute intervals for 10 minutes. At this point each subject was given one teaspoonful each of sodium bicarbonate and citric acid to produce CO₂ gas in the stomach. When sufficient gas and barium were present in the duodenum as indicated by fluoroscopy, X-ray films were obtained. At the completion of this study, pre- and post-medication films were reviewed and compared. The results of this study indicated that glucagon produced a highly significant (p<0.001) decrease in duodenal motility and toxicity when compared with placebo. There was also a significant response and a significant enhancement of the radiologist's ability to examine the duodenum by gas contrast after administration of glucagon as compared with administration of normal saline. Neither glucagon nor saline had any effect on the barium coating of the duodenal mucosa. Slight side effects were reported in four of the 10 patients. The results indicate that glucagon administration under these conditions could induce sufficient hypotonicity and hypomotility of the duodenum to provide a reliable demonstration of duodenal anatomy with minimal side effects.

In another similar study, Study I, glucagon (2 mg.) was compared to atropine sulfate (1 mg.) and to placebo in 12 asymptomatic subjects. In Study II, glucagon (2 mg.) was compared to propantheline bromide (30 mg.) and to placebo in another group of 12 asymptomatic volunteers. The medications were given double-blind and all subjects in each study received all drugs intramuscularly. Each subject was then given 1 cup of barium and the gastrointestinal tract observed fluoroscopically. After appropriate control films were obtained, medication was given. After medication administration, the stomach, duodenum, and small bowel were observed, both at 5 and 10 minutes. At 10 minutes the subject was given barium and solutions of bicarbonate and citric acid to produce gas in the stomach. Indicated films were obtained when sufficient gas and barium were present in the stomach and small bowel. At 30 minutes, the stomach and duodenal loop were observed and at 60 minutes a final film was obtained. A judgment of toxicity was made by a radiologist on the basis of the caliber and distensibility of the small bowel. The radiologist also determined whether examination of the upper gastrointestinal tract was enhanced by the medication and what effect, if any, the drug had on the barium coating of the gut.

The results indicated that, when compared to placebo, at 10 and 30 minutes, glucagon significantly (p<0.001) decreased the toxicity and motility of the stomach, duodenum, and small bowel. At 10 minutes, glucagon was also significantly (p<0.05) more effective than either atropine sulfate or propantheline bro-
mide. The duration of action of the drug was sufficient to allow the radiologist to complete his studies, yet the drug effects had dissipated by the time the subject left the X-ray department. Side effects of glucagon were minimal and were less than those reported following the use of propantheline bromide.

We claim:

1. The process of enhancing the visualization of the gastrointestinal tract which comprises administering to a patient 1 to 5 mg. of glucagon either intravenously or intramuscularly in conjunction with an effective amount of an X-ray contrast medium and then subjecting such treated patient to fluoroscopy or X-ray radiography.

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UNITED STATES PATENT OFFICE
CERTIFICATE OF CORRECTION

PATENT NO. : 3,862,301
DATED : January 22, 1975
INVENTOR(S) : Stanley H. Chernish, Roscoe E. Miller

It is certified that error appears in the above-identified patent and that said Letters Patent are hereby corrected as shown below:

On the Title page, column one, preceding item [22], insert --[73] Assignee: Eli Lilly and Company Indianapolis, Indiana--

Signed and sealed this 29th day of April 1975.

(SEAL)
Attest:

RUTH C. MASON
Attesting Officer

C. MARSHALL DANN
Commissioner of Patents and Trademarks