Intubation Studies of the Human Small Intestine:

XVII. The Effect of Atropine and Belladonna on the Motor Activity of the Small Intestine and Colon*

By

KENDALL A. ELSOM, M.D.

and

J. L. DROSSNER, M.D.†

IN spite of the well established pharmacologic observation that atropine depresses the motor function of the bowel its clinical use for that purpose has often been disappointing. We have consequently taken advantage of the technique of intestinal intubation, as developed in this clinic (1), and as previously employed by Abbott and Pendergrass (2) in a study of morphine, to determine objectively the effects of atropine and belladonna on the motor functions of the small intestine and colon of man. Both drugs produced a marked and lasting decrease in tone and motor activity of whatever portion of the tract was studied.

METHODS AND SUBJECTS

As previously described (2) the apparatus was introduced under fluoroscopic guidance to any desired portion of the tract. The balloon was then inflated with approximately 40 cc. of air under 10-12 cm. of water pressure and connected with a spirometer type of volume recorder which activated a writing lever. In some instances a suspension of barium was introduced to permit simultaneous fluoroscopic observation of the calibre and motor activity of the bowel immediately proximal or distal to the inflated balloon. The method employed in these experiments has limitations discussed by Abbott (2). If the balloon enters a constricted portion of the gut, or is impinged upon by a bolus of intestinal contents the writing lever may indicate an increase in tone which is fictitious. Simultaneous fluoroscopic study usually discloses the fact, however, and therefore serves as a control of this part of the method. No technical errors now recognized produce an apparent fall in tone.

Except for 3 individuals who had abnormalities considered suitable for study all the subjects were without demonstrable gastro-intestinal disease. Two of the three showed small intestinal hypermotility and hypertonicity by roentgen examination and a third had ulcerative colitis for which an ileostomy had been performed. This latter subject provided an opportunity for simultaneous intubation through the ileostomy opening of the terminal ileum and the colon. In all subjects control tracings of intestinal activity were obtained before atropine sulphate was injected hypodermically. In a few instances atropine or belladonna was administered orally.

ACTION ON THE DUODENUM

Eight observations were made on 5 subjects. The control tracings from the normal duodenum have two chief characteristics: The intestinal tone is high and the motor activity is great. Two types of waves are recorded as a rule, large peristaltic waves occurring every minute or two and lasting approximately a minute, on which are superimposed frequent small undulations produced by rhythmical contractions.

Administration of atropine sulphate was followed (Fig. 1) in 10 to 15 minutes by a gradual fall in intraduodenal tone. The large peristaltic contractions were altered simultaneously, often becoming more pronounced as the tone decreased, then gradually diminishing in size and frequency and ultimately disappearing. The small rhythmical waves were decreased in size though usually not in frequency. This effect of atropine was fully developed within 20 minutes

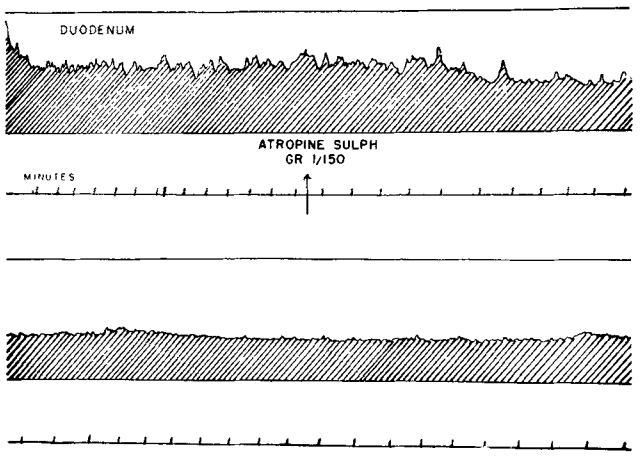

Fig. 1. The effect of atropine on the duodenum. In this and the following figures the upper horizontal line represents the position of the writing lever when the balloon is empty, the base line its position when the balloon contains 40 cc. of air. Time in minutes.

after the injection, and lasted for 1 to 2 hours. Recovery was gradual, with first an increase in size of the small undulations, then the appearance of peristaltic waves and finally an increase in tone.

ACTION ON THE JEJUNUM AND ILEUM

The results of 6 experiments on the jejunum and 3 on the ileum are here considered together since the tracings obtained from these portions of the bowel are similar to each other and rather different from those obtained from the duodenum. In the control tracings taken from these portions of the bowel the high tonus and the marked motor activity which characterize the duodenum diminish progressively as the balloon descends into the more distal segments of the small bowel. The large, relatively infrequent peristaltic

*From the Gastro-Intestinal Section (Kinsey-Thomas Foundation) of the Medical Clinic, Hospital of the University of Pennsylvania.
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†Smith, Kline and French Fellow in Gastro-Enterology.

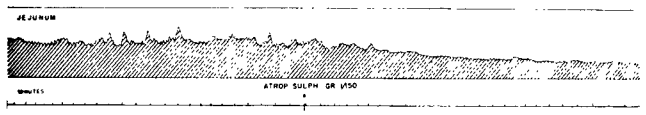


Fig. 2. The effect of atropine on the jejunum.

waves characteristic of the duodenum are inconspicuous in tracings from the jejunum. The small, rhythmic undulations are often the only evidence of motor activity. The effects on the jejunum and ileum produced by atropine were perhaps less striking than those on the duodenum but were no less definite. Fig. 2 shows a representative tracing obtained from the upper jejunum of a normal subject. The first detectable effect was a moderate decrease in intestinal tone. The character of the waves then gradually changed. The larger peristaltic waves decreased and ultimately disappeared, while the rhythmical contractions became smaller, but increased in frequency. The effect of atropine on the ileum in normal subject is seen in Fig. 3. In this instance a suspension of barium had been introduced proximal to the inflated balloon. This procedure altered the type of control record normally obtained from this section of the gut. Large con-

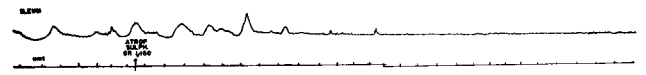


Fig. 3. The effect of atropine on the ileum.

traction waves on which small undulations were superimposed occurred every 1 or 2 minutes and lasted approximately 1 minute. The effect of atropine is clearly apparent. Ten minutes after its injection the tracing was a straight line, except for small, rapid rhythmical waves.

Fig. 4 shows a tracing from the jejunum of a patient, (Mrs. E. R.) whose case history is summarized below. It is abnormal in two respects: the tonus is higher than that customarily found in the jejunum, and the motor activity, with fairly large peristaltic waves, is unusually great. The effect of atropine (0.6 mg.) was striking. A decrease in tonus occurred within 10 minutes after the injection while the peristaltic waves were as large or larger than those in the control period. Within 20 minutes after the injection, the peristaltic waves were absent and the small undu-

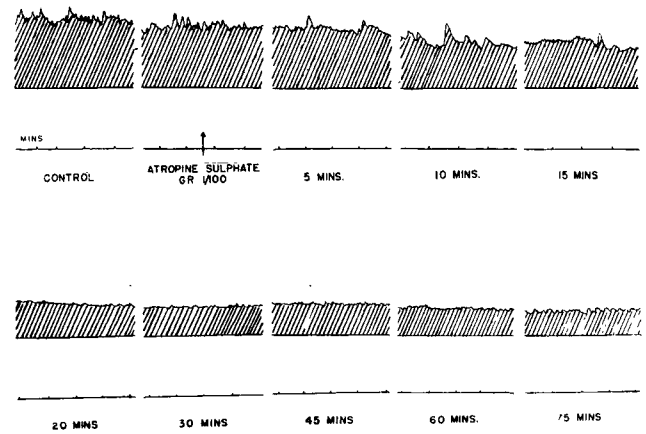


Fig. 4. The effect of atropine on the jejunum of a subject with small intestinal hypermotility and hypertonicity.

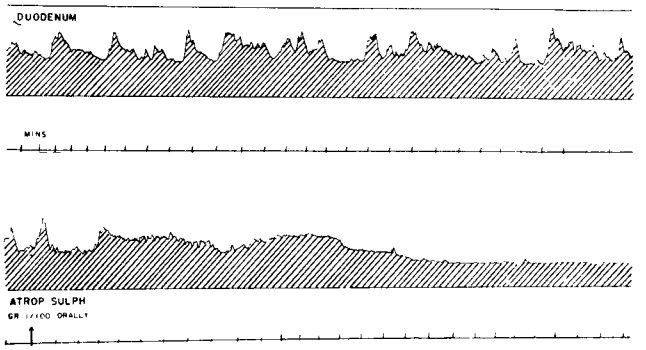


Fig. 5. The effect on the duodenum of atropine administered orally.

lations were greatly decreased in size. Seventy-five minutes after the injection the latter waves had increased in prominence, but peristalsis was still absent and the tonus was greatly diminished.

ACTION ON THE COLON

Four observations were made. In 2 normal subjects the effects were only slight, consisting in a decrease in tone and reduction in motor activity. In these two instances the colon was relatively inactive during the control period and interpretation of the effects of

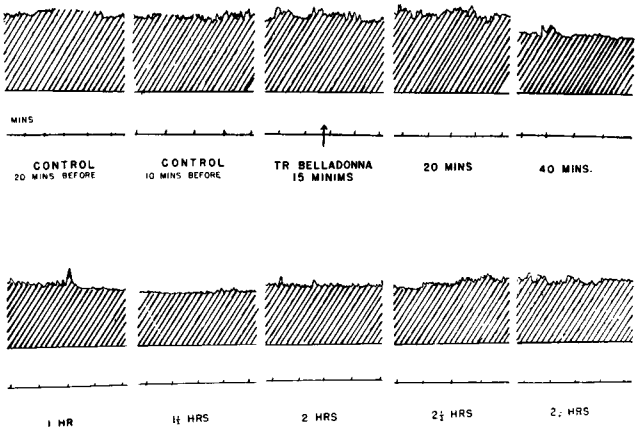


Fig. 6. The effect on the jejunum of Tr. Belladonna administered orally.

atropine was difficult. In the subject with ulcerative colitis the contractions of the colon were abnormally frequent and here the anti-spasmodic action of atropine was clearly apparent. Fig. 7 shows the record obtained from a patient with partial obstruction in the sigmoid region. The control tracing, obtained from the cecum, records frequent large contraction waves which expelled most of the air from the balloon. No such waves appeared after the administration of

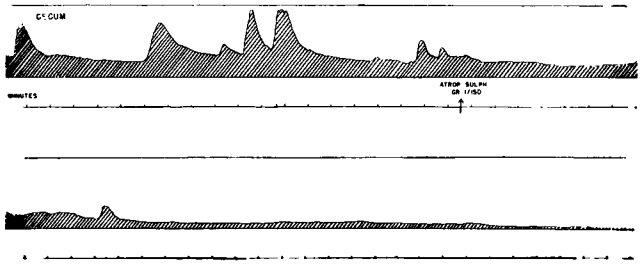


Fig. 7. The effect of atropine on the colon of a subject with partial colonic obstruction.

atropine (0.4 mg.) and the tonus was definitely diminished.

EFFECTS OF ORAL ADMINISTRATION

Atropine sulphate (Fig. 5) and tincture of belladonna (Fig. 6) orally administered produced effects qualitatively similar to those already described for hypodermic injection. The effects were slower in onset, appearing as late as 30 minutes after administration of the drug, and were less marked and less prolonged than from a similar dose administered subcutaneously.

DURATION OF ACTION

The decrease in the peristaltic and rhythmical contractions produced by 0.4 to 0.6 mgm. of atropine sulphate persisted as a rule for 1½ to 2 hours, with gradual return to normal. The effect on intestinal tone was more lasting. In Fig. 6 for example, the tone was still decreased 2 hours after administration of the drug although the contraction waves had returned to their normal size. Because of lack of time most of the observations had to be discontinued while the tone was still abnormally low.

THE EFFECT OF ATROPINE ON SMALL INTESTINAL MOTILITY

The marked decrease in motor activity observed in all portions of the intestine after atropine prompted a study of the rate of passage of the usual barium meal through the small bowel. It is generally agreed that atropine delays gastric emptying (3). Since the rate at which barium leaves the stomach in part determines the speed of its propulsion through the small intestine, the factor of gastric emptying was eliminated as follows: A normal subject was intubated with a Rehfuss tube, the tip of which was observed to lie in the third portion of the duodenum. In an effort to simulate conditions of normal gastric emptying 175 cc. of a barium suspension were introduced into the duodenum in 7 divided doses of 25 cc. each, injected at 15 minute intervals. The rate of passage of the meal was carefully determined by frequent fluoroscopic examinations. One week later the procedure was repeated under identical conditions except that atropine sulphate (0.4 mgm.) was injected subcutaneously 10 minutes before the introduction of the barium, and 0.2 mgm. was injected 1 hour and 45 minutes following it. Table I indicates the observed differences in motility. The following observation of the effect of atropine in a patient with abnormally rapid small intestinal motility appears to be of practical value:

TABLE I

Small intestinal motility before and after the injection of 0.4 mgm. of atropine sulphate

Hours After Introduction of Barium Into Duodenum	The Position of the Barium Meal	
	Without Atropine 2/18/39	With Atropine 2/25/39
½	Chiefly in the upper jejunum.	Entire meal in first few inches of jejunum.
1	In ileal loops situated in pelvis and right lower abdominal quadrant.	Entire meal in duodenum and first two jejunal loops.
1½	Position of head of column not materially changed. most of the barium in mid-jejunum.	Head of the meal in distal jejunum. Most of barium in proximal jejunum.
2	No appreciable change in past half hour.	No appreciable change in the past half hour.
2¾	Head of meal at hepatic flexure of colon. Most of barium in terminal ileum. Observations discontinued.	No appreciable change.
3		No appreciable change.
4		Most of barium in proximal loops of ileum, none in loops situated in pelvis.
5		All of the barium now in the lower ileum, head of column just entering terminal ileum.
5½		Head of column has just reached the cecum.

E. R. (No. 39-37, 955) a white woman, aged 50, complained of diarrhea of 12 years duration. She passed from 5 to 10 stools daily. Flatulence and mild abdominal pain often preceded the passage of the stools, which were liquid or semi-solid. Tenesmus was marked. She was a chronic invalid because of marked asthenia.

Physical examination was negative. Hemoglobin was 74 per cent (Sahli). Extensive laboratory tests were negative. Proctoscopic examination and repeated stool examinations revealed nothing of significance.

Gastro-intestinal roentgen examination disclosed a hypertonic small intestinal pattern with marked hypermotility. At a second examination 3 days later, atropine sulphate (0.4 mgm.) was administered hypodermically 7 minutes before the barium was swallowed, and the dose repeated in 2 hours. The resulting delay in gastric emptying time, the decreased small intestinal motility and the altered pattern are illustrated in Fig. 8.

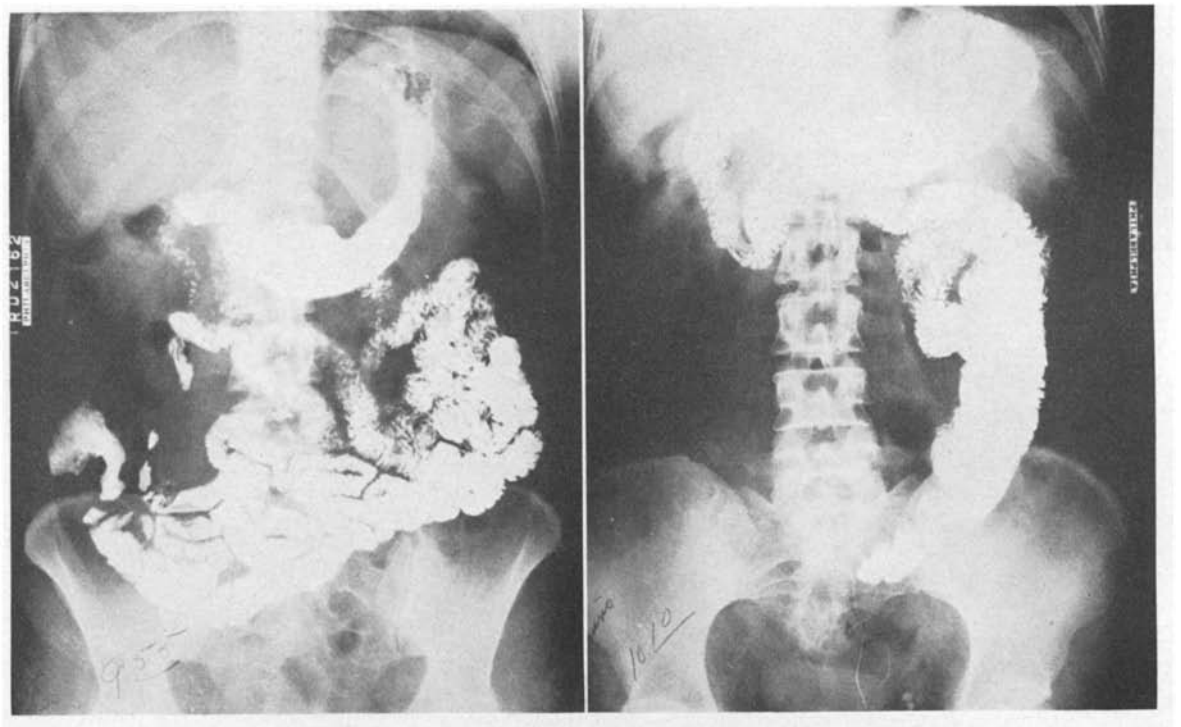
Twenty drops of tincture of belladonna were administered therapeutically 3 times daily. The diarrhea immediately ceased, one or two formed stools being passed daily, and she stated that she had not felt so well for 10 years. For a two day period, when she was unable to obtain the drug, the diarrhea reappeared, only to disappear when medication was resumed.

DISCUSSION

The effects produced by atropine in the human small intestine and colon are definite. Under the conditions of our experiments the tone is lessened, the muscular contractions are diminished, and, as a result, intestinal motility is decreased. The results were uniform and dependable. In 21 observations the action was marked in 14, moderate in 8, slight in 1, and absent in only 1. These results are in general agreement with evidence derived from the small intestine of animals (4), and the stomach (5, 6) and colon (7) of man.

The statement of Cushny (8) that "small (therapeutic) doses of atropine appear to arrest only certain abnormal violent forms of contraction" has not been borne out in our experiments on man, since both abnormal contractions and those observed in the normal bowel were equally affected. The statement of Bastedo (9) that "in doses usually employed by mouth or permissible for any continued treatment, atropine and belladonna are practically without effect on the secretory and motor functions of the stomach" cannot be applied to the small intestine and colon.

While it is true that a balloon occluding the bowel creates an abnormal situation it is impossible to say whether it reproduces any observed clinical disturbances. This uncertainty, however, does not, in our opinion, invalidate the general conclusion that the ob-



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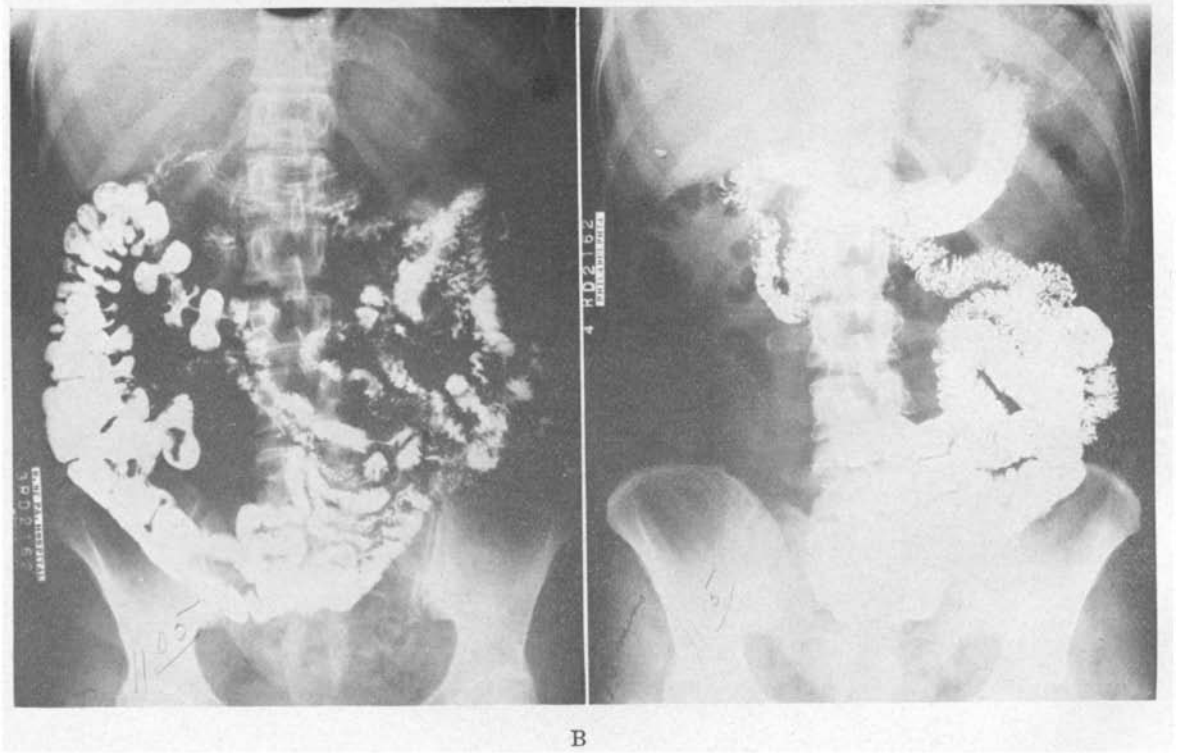

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served decrease in both tone and muscular activity of the intestinal tract produced by doses of atropine which are well tolerated can properly be expected to produce useful results.

CONCLUSIONS

Atropine sulphate and tincture of belladonna have been administered to normal subjects and patients with gastro-intestinal disease and their effects on the small intestine and colon studied by means of intestinal intubation combined with fluoroscopy.

In therapeutic doses they produce definite and prolonged effects on the small bowel and colon consisting of a marked decrease in tone and in peristaltic activity and of a less striking effect on rhythmical contractions.

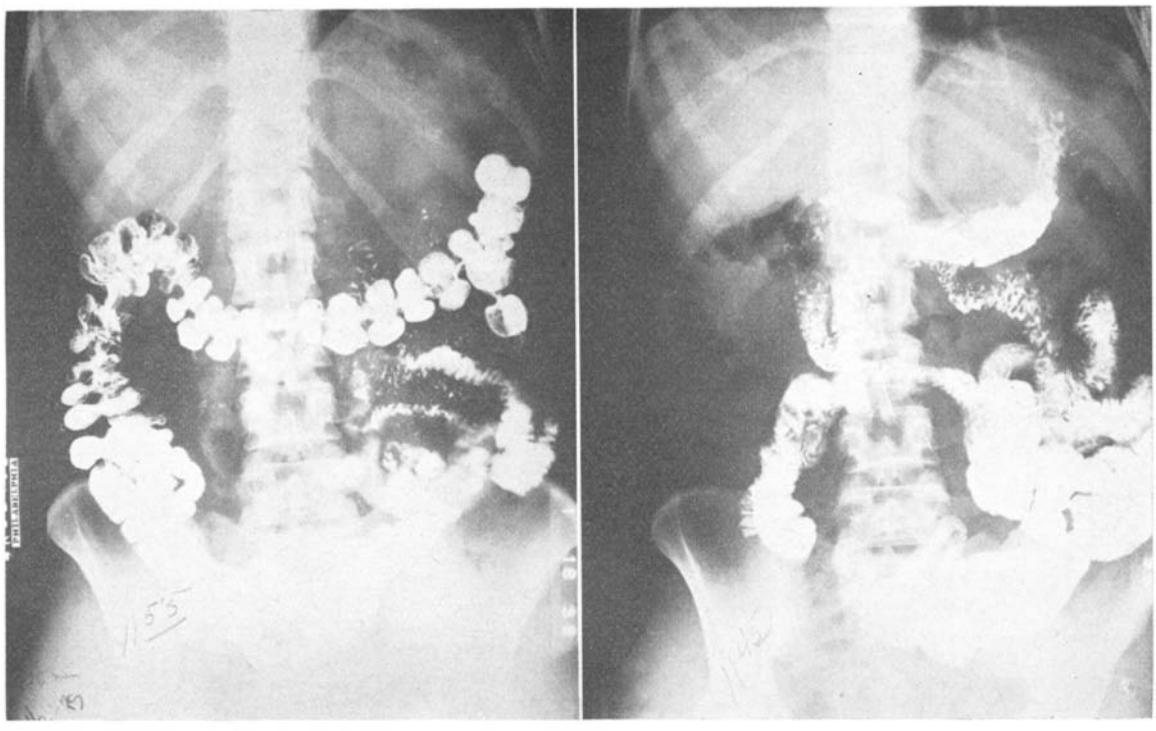

Fig. 8. The effect of atropine on small intestinal hypermotility and hypertonicity. Left hand column, before atropine. (a) 25, (b) 95 and (c) 145 minutes after a barium meal. Right hand column, after atropine. (a) 20, (b) 90 and (c) 120 minutes after a barium meal.

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Intubation Studies of the Human Small Intestine:

XVIII. The Effect of Pitressin and of Amphetamine (Benzedrine) Sulphate on the Motor Activity of the Small Intestine and Colon*

By

KENDALL A. ELSOM, M.D., PAUL M. GLENN, M.D.†

and

J. L. DROSSNER, M.D.‡

IN the present study the technique of intestinal intubation has been utilized to determine the effects on the human small intestine and colon of pitressin and amphetamine (benzedrine) sulphate. Similar studies of morphine (1) and of atropine (2) have been reported from this clinic. The method of intestinal intubation makes possible the objective demonstration of drug effects on portions of the intact human intestinal tract hitherto inaccessible, and permits evaluation in man rather than in laboratory animals of the uses and limitations of drugs.

Methods and Subjects

The method of intestinal intubation as developed and carried out in this clinic (3) requires no further description here. It permits the introduction to any

*From the Gastro-Intestinal Section (Kinsey-Thomas Foundation) of the Medical Clinic, Hospital of the University of Pennsylvania, Philadelphia.

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†Formerly Justice M. Thompson Fellow in Gastro-Enterology.

‡Smith, Kline and French Fellow in Gastro-Enterology.