

CLINICAL AND ROENTGENOLOGIC EVALUATION OF BANTHINE ON THE MOTILITY OF THE COLON

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INTRODUCTION

BANTHINE is an anticholinergic drug and is known chemically as a methantheline bromide. Longino, Grimson, Chittum and Metcalf (1) indicate that Banthine has an atropine-like action as is shown in preventing contraction of strips of excised rabbit ileum when stimulated by acetylcholine, and has autonomic ganglion blocking action on the sympathetic and parasympathetic system; it also exerts an atropine-like action at the post-ganglionic nerve endings of the parasympathetic system.

Kern and Almy (2) made studies on colonic activity in normal human beings by obtaining tracings of pressure changes in balloons inserted into the colon; they concluded that oral administration of 100 mgm. of Banthine reduces normal colonic activity 15 minutes after ingestion of the drug and that it continues for more than two hours.

Individual clinical reports showing that Banthine decreases colonic contractions were made by Kern, Almy and Stock (3) and by Plummer, Burke and Williams (4). Our interest was directed primarily toward the effects of Banthine upon the motility of the colon on a large group of patients.*

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PROCEDURE AND METHODS

We have selected one hundred patients with disease of the colon and studied them clinically and roentgenologically. The group comprised 27 patients having constipation, 46 patients having ulcerative colitis, 7 patients having spastic colitis and 10 patients with permanent ileostomies following total colectomies. Normal controls were also included in this series. Patients were either hospitalized or studied ambulatorily. Evaluation of the motility of the colon was made clinically by determining the variation in the average number of stools daily before and after Banthine, by the presence or absence of abdominal pain and cramping (referable to the colon), and by the presence or absence of blood in the stool.

Roentgenologically a comparison was made determining the variation in the emptying time of the colon in hours before and after oral administration of Banthine. A standard amount of barium was given to each patient by mouth. Barium progress was visualized daily by continuous fluoroscopy and by repeated films.

In each patient, the study was made during the first week clinically and roentgenologically without administration of Banthine; during the second week similar studies were repeated after oral administration of 50 mgm. of Banthine four times daily. Upon completion of the 2 week study with roentgenologic evaluation of the motility of the colon, clinical studies were continued for 90 days in each patient, only the Banthine was decreased to 50 mgm. three times daily. The averages recorded in Table III are averages for one day.

RESULTS

In the clinical evaluation the results were classified

TABLE I

SHOWING VARIATIONS IN THE NUMBER OF STOOL EVACUATIONS BEFORE AND AFTER INTAKE OF BANTHINE

CLINICAL RESULTS ON 100 PATIENTS

No. of Pts.	Diagnosis	Average Number of Daily Evacuations																				
		Before Banthine											During Banthine									
		0	1	2	3	4	5	6	7	8	12	15	Av.	0	1	2	3	4	5	6	7	Av.
27	Constipation	16	9 ^a	2 ^b									2	19	7	1						1
46	Chronic Ulcerative Colitis	1	9	9	3	6	5	8	1	2	2	5	2	25	14	5						1
7	Spastic Colitis	2	2	1	2							2	2	5								1
10	Ileostomies	By Ileostomy 9 1 Bag											4		10						2	
10	Normal Controls	10										2	4	6								1

a, b) The average evacuation reported weights from 2 to 4 Grams.

EFFECT OF BANTHINE ON MOTILITY OF COLON

TABLE II

SHOWING VARIATIONS IN MOTILITY AS UNCHANGED, HASTENED OR DELAYED AFTER INTAKE OF BANTHINE. (BASED ON THE EMPTYING TIME OF THE COLON IN HOURS BEFORE AND DURING BANTHINE)

ROENTGENOLOGIC RESULTS ON 100 PATIENTS

No. of Pts.	Diagnosis	Emptying time of Colon		During Banthine			
		Av. emptying time in hours	Before	During	U*	H	D
27	Constipation		77	113			100%
46	Chronic Ulcerative Colitis		62	101			100%
7	Spastic Colitis		68	120			100%
10	Ileostomies			NO STUDIES MADE			
10	Normal Controls		72	108			100%

*U—unchanged; H—hastened; D—delayed.

as variations in the number of stool evacuations daily before and after intake of Banthine.

In Table I, we show these variations in 27 patients with constipation, 46 patients having ulcerative colitis, 7 patients with spastic colitis and 10 patients with permanent ileostomies following total colectomies. Normal controls are also included in this table.

In the roentgenologic evaluation, the results were classified as variations in the emptying time of the colon in hours before and after Banthine. These variations are expressed in Table II. This table incorporates the roentgenologic studies of the same group of patients recorded in Table I.

In Table III a summation of clinical results is shown expressing variations in motility of the colon as unchanged, hastened or delayed.

In Table II a summation of the roentgenologic results is shown expressing variations in motility of the colon as unchanged, hastened or delayed.

In the summation of the results roentgenologically we were interested in determining the variations in

the emptying time of different anatomical portions of the colon. We are, therefore, presenting Table IV.

DISCUSSION: CLINICAL EVALUATION

The laboratory experiments of Longino, Grimson, Chittum and Metcalf (1), by Kern and Almy (2), by Kern, Almy and Stock (3) and by Plummer, Burke and Williams (4) are substantiated by many clinical reports. Segal (5) in using 100 mgm. of Banthine every six hours in 3 patients with regional enteritis found the patients were relieved of their pain and diarrhea.

Golden (6) reported that two patients with ulcerative colitis, diarrhea, abdominal pain and loss of weight were relieved after intake of 100 mgm. of Banthine every six hours.

Kern, Almy and Stock (3) in investigating the motility of the sigmoid in 23 normal subjects by kymographic recordings of pressure changes in inlying balloons, state that 100 mgm. given orally completely abolishes sigmoid motility for prolonged periods. They report that in diarrheas the number of movements de-

TABLE III

SHOWING VARIATIONS IN MOTILITY AS UNCHANGED, HASTENED OR DELAYED AFTER INTAKE OF BANTHINE. (BASED ON AVERAGE NUMBER OF EVACUATIONS DAILY BEFORE AND DURING BANTHINE)

CLINICAL RESULTS ON 100 PATIENTS

No. of Pts.	Diagnosis	Emptying Time of Colon		During Banthine			
		Ave. No. of Evacuations Daily	Before	During	U*	H	D
27	Constipation		2	1	2		25
46	Chronic Ulcerative Colitis		5	1	4		42
7	Spastic Colitis		2	1			7
10 ^a	Ileostomies		4	By Ileostomy Bag			10 ^a
10	Normal controls		2	1			10

*U—Unchanged; H—Hastened; D—Delayed; a—This refers to evacuation of ileostomy.

TABLE IV
SHOWING VARIATIONS IN EMPTYING TIME (IN HOURS) OF THE CECUM, TRANSVERSE
COLON AND SIGMOID BEFORE AND AFTER INTAKE OF BANTHINE
ROENTGENOLOGIC RESULTS ON 100 PATIENTS

No. of Pts.	Diagnosis	Emptying Time in Hours					
		Before Banthine			During Banthine		
		Cecum	Transv. Colon	Sigmoid Rectum	Cecum	Transv. Colon	Sigmoid Rectum
27	Constipation	19	39	77	43	73	113
46	Chronic Ulcerative Colitis	11	33	62	29	61	101
7	Spastic Colitis	14	45	68	34	84	120
10	Ileostomies	NO STUDIES MADE					
10	Normal Controls	12	38	72	31	69	108

creased, the stools became less liquid, the amount of mucus diminished and that the urgency was less.

Plummer, Burke and Williams (4) also report that four of five patients who had non-specific colitis appeared to obtain relief from abdominal cramps on a dosage of 150 to 200 mgm. of Banthine.

McHardy, Browne, Marek, McHardy and Ward (8) report that hypermotility, diarrhea in amebiasis, tuberculous cecitis, chronic ulcerative colitis and lymphopathia venereum were not influenced, and that actual colon disease entities were not influenced by Banthine; they also report that in severe irritable colon syndrome methantheline in doses of 400 mgm. daily had a limited but appreciably favorable effect. Apparently their estimations of the efficacy of Banthine in the colon are entirely subjective.

In the evaluation of our studies, we find parallelism in the results obtained by the individual reports made by other investigators. Our attention was directed primarily toward clinical and roentgenologic evaluation of Banthine in common diseases of the colon. We have studied a large group of patients with constipation, chronic ulcerative colitis, spastic colitis, patients with permanent ileostomies (individuals who have frequent evacuations of liquid consistency) and also included studies on a group of normal individuals (individuals who do not have diseases of the colon).

In Table I, it is apparent that the group of patients with constipation averaged two stools daily before intake of Banthine and that the number of evacuations was decreased to 1 daily after oral intake of 50 mgm. of Banthine 3 to 4 times daily. The averages recorded are daily averages. The patients with constipation who have reported as having 2 stools daily were reporting stools of very small quantities (weighing from 2 to 4 grams per stool). The average normal stool passage weighs about 100 grams.

In patients with ulcerative colitis we found that the number of daily evacuations decreased from an average of 5 to an average of one. This finding parallels the decrease of blood in the stool after Banthine. The favorable clinical results with Banthine were sustained only upon continual use of Banthine; four patients did not respond to Banthine.

The pain and cramping in the lower abdominal region is decreased considerably after prolonged intake of Banthine. Dosages of 50 mgm. 3 to 4 times daily are sufficient to produce optimum results if used over prolonged intervals followed by a period of rest.

In spastic colitis the degree of spasms has been alleviated considerably and in 4 patients the spasms in the lower abdomen have subsided entirely.

We were gratified in the results obtained in patients with permanent ileostomies; by the use of Ban-

TABLE IV A
SHOWING THE RANGE IN EMPTYING TIME (IN HOURS) OF THE CECUM, TRANSVERSE
COLON AND SIGMOID BEFORE AND DURING INTAKE OF BANTHINE
ROENTGENOLOGIC RESULTS ON 100 PATIENTS

No. of Pts.	Diagnosis	Emptying Time in Hours					
		Before Banthine			During Banthine		
		Cecum	Transv. Colon	Sigmoid & Rectum	Cecum	Transv. Colon	Sigmoid & Rectum
27	Constipation	7 to 48	24 to 72	72 to 120	24 to 72	68 to 96	96 to 144
46	Chronic Ulcerative Colitis	4 to 24	7 to 48	24 to 96	7 to 96	24 to 96	96 to 144
7	Spastic Colitis	7 to 24	24 to 96	60 to 120	24 to 72	72 to 120	114 to 144
10	Normal Controls	7 to 24	24 to 48	48 to 96	24 to 48	48 to 96	96 to 120

TABLE V
SHOWING DELAY OF EMPTYING TIME OF COLON IN PERCENT HOURS

No. of Pts.	Diagnosis	Before Banthine			During Banthine			Percent Delay with Banthine		
		Cecum	Transv. Colon Time in Hours	Sigmoid & Rectum	Cecum	Transv. Colon Time in Hours	Sigmoid & Rectum	Cecum	Transv. Colon	Sigmoid & Rectum
27	Constipation	19	39	77	43	73	113	126	87	47
46	Chronic Ulcerative Colitis	11	33	62	29	61	101	163	85	63
7	Spastic Colitis	14	45	68	34	84	120	143	86	76
10	Normal Controls	12	38	72	31	69	108	160	81	50

thine of 50 mgm. two to three times daily we were able to change the consistency of the numerous evacuations from a liquid to a semiformal condition and were able to reduce the number of evacuations. While ileostomies are not considered as diseases of the colon we are including this group as a control group in comparing the results obtained in conditions of the colon that produce diarrheas.

UNTOWARD EFFECTS

The patients have noted only minor discomfort following intake of 50 mgm. of Banthine 3 to 4 times daily over continual usage of this drug for 2 to 3 months uninterruptedly. In the entire group of patients studied, one patient reported mild dryness of the throat only on the 4th day, the second patient noted a soreness of the mouth and the third patient reported a burning or an itching of the rectum lasting from the 2nd to the 4th day of intake. These disturbances were mild and did not require any treatment and did not require discontinuance of Banthine therapy.

In summation of our clinical observations, the impression we have is that Banthine delays motility of the colon and that it accomplishes these results very effectively. Since spasms of the colon are spasms of smooth muscle and since smooth muscle spasm is neural in origin one therefore assumes that such spasms are the result of transmission of neural stimuli to smooth muscle through the medium of acetylcholine.

Benson, Schwartzman, Green and Reed (7) amplify the fact that Banthine therefore acts as an anticholinergic drug through its ability to inhibit the transmission of neural stimuli at the sites where acetylcholine serves to transmit the impulse.

ROENTGENOLOGIC EVALUATION

To verify the clinical results obtained in these patients we applied standard methods of roentgenologic procedures in evaluating variation in motility of the colon before and after Banthine. The criterion used is the emptying time of the colon in hours after intake of barium meal and obtaining a comparison of the emptying time before and after intake of Banthine. We were also interested in determining if possible which anatomical portion of the colon is primarily responsible for the delay in the motility of the colon.

In Table II, the results show that in 27 patients with constipation the emptying time of the colon in hours is delayed after intake by 36 hours.

The emptying time of the colon in 46 patients with chronic ulcerative colitis is delayed by 39 hours. Parallel results in emptying time of the colon were noted in patients with spastic colitis and in the normal controls.

The patients with ileostomies presented inconsistent results in emptying time of the ileostomy roentgenologically and it is, therefore, that we cannot correlate the findings in this group except by clinical observations.

In 27 patients with constipation the emptying time of the cecum was delayed by 24 hours after Banthine, and the emptying time of the transverse colon was delayed by 34 hours, while that of the entire colon was delayed by 36 hours.

In 46 patients with chronic ulcerative colitis similar comparisons are made of the emptying time of the cecum, the transverse colon and the entire colon. Parallel results in the delay of the emptying time of the cecum, of the transverse colon and of the entire

TABLE VI
SHOWING EMPTYING TIME OF COLON IN PERCENT OF PATIENTS

No. of Pts.	Diagnosis	Before Banthine			During Banthine		
		Cecum	Transv. Colon	Sigmoid & Rectum	Cecum	Transv. Colon	Sigmoid & Rectum
		Less than 24 hours	Less than 48 hours	Less than 72 hours	More than 24 hours	More than 48 hours	More than 72 hours
27	Constipation	44	41	29	63	80	88
46	Chronic Ulcerative Colitis	67	52	48	96	64	70
7	Spastic Colitis	60	30	20	100	60	100
10	Normal Controls	70	40	10	100	70	100

colon are noted in patients with spastic colitis and in the normal controls.

Making a comparative analysis in determining which anatomical segment of the colon presents the optimum delay in motility we can make the following observation: The cecum presents the optimum delay in the consideration of segmental delay, this is shown in Table V and Table VI.

CONCLUSIONS

1. By clinical observations Banthine delays motility of the colon in patients who have constipation, chronic ulcerative colitis, spastic colitis, ileostomies, and normal persons.

2. By roentgenologic observations, Banthine delays motility of the colon in the same group of patients studied clinically.

3. By roentgenologic evaluations, the optimum delay in the motility of the colon is noted in the cecum.

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OBSERVATIONS ON A METHOD FOR SUSPECTING THE PRESENCE OF ACTIVE DUODENAL ULCER BY PHYSICAL EXAMINATION

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THE ATTITUDE of the physician in 1910 toward the diagnosis of peptic ulcer was summarized by the following quotation from the writing of Moynihan (1): "The symptoms so perfectly characteristic of duodenal ulcer may be present for years without producing any physical signs. It is, therefore, not necessary to the attaining of an accurate diagnosis that any physical examination of the patient be made. The anamnesis is everything, the physical examination relatively nothing."

In the ensuing years, however, Boas (2), Mendel (3) and Jacob Meyer (4) suggested physical diagnostic signs based upon the elicitation of a painful response following pressure on the 11th to 12th thoracic vertebrae, or following pinching or percussion of the epigastric area. These signs did not find wide acceptance, probably because of the variability of the responses that were obtained. Other writers refer to epigastric tenderness as a fairly frequent finding, but again, acknowledge the unreliability of subjective responses. To this date, textbooks in the fields of Internal Medicine, Surgery, Gastroenterology, and Physical Diagnosis quite universally quote Moynihan's dictum: "The anamnesis is everything, the physical examination relatively nothing" (5-19).

The diagnosis, it is true, may readily be suspected when the history is "classical," but such histories are quite uncommon. There are remarkable variations in perceptiveness of subjective phenomena. The inability

to formulate subjective experiences into verbalizations may prevent adequate communication with the physician. Pain thresholds vary considerably. Patients may minimize or deny the existence of symptoms to serve particular psychic needs. Laterally, the symptom-masking effects of the newer hormone and steroids (ACTH, Cortisone, etc.) have become well known, and in selected cases, histories of gastrointestinal abnormality may be entirely absent until hemorrhage or perforation has occurred.

The physical examination, in light of observations here to be reported, has proven to be of inestimable value in suspecting the presence of active peptic ulcer, regardless of the patient's history.

PATIENT SELECTION AND METHOD OF PHYSICAL EXAMINATION

Consecutive unselected patients, the variety of practice usually seen by an Internist, constituted the subject material upon which this study was based. The ages varied from 16 to 76. There were 100 patients in the series.

The method used was as follows: The patient was placed on an examining table in a semi-reclining position, arms resting comfortably at the sides, knees drawn up. Abdominal relaxation was encouraged as much as possible. The examiner first palpated the lower quadrants, using a bilateral but alternating pressure, then slowly approached the epigastric region.