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Pathologic physiology of the colon : with special reference to intestinal stasis

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PATHOLOGIC PHYSIOLOGY OF THE COLON

With Special Reference to Intestinal Stasis

By

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Dedicated to A. D. C.

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I. INTRODUCTION

Therapeutics today should be based upon the physiology of the organism and the pathological changes of that physiology. The progress of medicine through the centuries has shown a gradual departure from imperialism in therapy, this always being replaced by rational and logical treatment as physiology and altered physiology became better understood. As a layman I was always impressed and confused concerning constipation because of the vast numbers of divergent opinions and alleged remedies for the condition. After becoming affiliated with the medical profession this confusion was only partially relieved, and as I learned of the divergent medical opinions relative to the functions of the digestive tract, and particularly the colon, I was lead to attempt this resume of recent authoratative information on the subject. I feel that only by a better understanding of the physiology of the gastrointestinal tract and the altered physiology associated with intestinal stasis can one become more nearly proficient in treatment.

II. EMBRYOLOGY

Developmentally, anatomically and physiologically the right and left halves of the colon differ so much that it is virtually a dual organ. The right or proximal half develops with the small bowel, its caliber is large, its function is absorptive, and its content is more or less liquid. The left or distal half develops with the rectal portion of the intestine, its caliber is relatively small, it has little absorptive power, its function is storage, and its contents are usually more or less solid. (22)

The colon in fetal life is normally a mid-line vertical tube affixed to the spine by peritoneal ligamentous attachments. This primative gut becomes divided into three functioning parts: 1. the foregut deriving its blood supply from the celiac axis, and comprising that portion of the digestive apparatus from the pharynx to the duodenum at the point of entry of the common bile duct; 2. the mid-gut, deriving its blood supply from the superior mesenteric artery, and comprising that portion of the digestive tract which has to do with absorption, extending from the entry of the common bile duct to approximately the middle

of the transverse colon; and 3. the hind-gut, supplied by the inferior mesenteric artery and comprising the large bowel from the middle of the transverse colon to the junction of the rectum with the anus. (77)

About the third month of intrauterine life the colon still lies to the left of the mid line. Shortly thereafter, from its low point of development it rotates on the superior mesenteric artery and ascends in the abdomen and goes to the right side, coming to lie, at about the fourth month under the surface of the liver. It normally sinks to its semiflexed position in the right iliac fasca, beginning its descent about mid-fetal life and is not completed until early childhood. (6) Non or incomplete rotation may take place and the cecum may be stopped in its course at any point from the left to right along the route it normally traverses.

The rectum is derived from the cloaca, a highly differentiated extention of the hind-gut (third embryonal week). From the cloaca the genito-urinary system also develops. Caudally the cloaca extends to form the post-allantoic intestine or primitive rectum. The primitive genito-urinary system and rectum became

separated by a saddle-like down growth which ultimately becomes the perineum. The final stage in completion of the one tube digestive tract is the absorption of the intervening mesoblastic membrane between the proctodeum (anlage of the anal canal) and the developing rectum, and the fusion of their mucosal surfaces. The anal plate, formed by the fusion of the ectoderm, cloacal endoderm and mesodermal partition, likewise becomes absorbed leaving the patent anal canal. (77)

Keith (51) states that both the sphincter muscles are developed in connection with the proctodeum and fixes the upper limit of this origin at the upper of the columns of Morgagni. It may be noted that in carcinoma or infections of this region the inguinal nodes are liable to be involved as well as the perirectal ones since the proctodeum carries its lymphatic structures with it.

III. ANATOMY

In general, only significant points related to intestinal stasis will be attempted to be given here. For general and detailed anatomy the reader is referred to a text on the subject. As intestinal stasis is generally concerned with the terminal one foot or eighteen inches of the colon a more detailed anatomical consideration will be given to this region. As stasis results, though comparatively rarely, from hyper or hypo function the ileo-cecal sphincter it will be briefly considered.

In 1579 Casper Bauhin discovered the ileo-cecal sphincteric action, and Keith in 1903 first reported the presence of an anatomical muscular thickening of the transverse layer muscle of the colon where it joins the ileum. (77) Normally it prevents food from entering the colon before nutrient material has been fully absorbed by the ileum as well as preventing reflux of colomic content back into the ileum. Hertz (43) points out that while this is normally true, patency of this structure is often found without giving symptoms, and that the terminal ileum is very active in peristolsis and food is quite forceably propelled into the cecum which at this time is very quiet and fills

passively, even including the entire ascending colon. Iliac stasis actually occurs by irritation and spasm of this sphincter as in such conditions as peritoneal or intestinal inflammations. In cases of patency of the sphincter it seems plausible that incompletely digested food would be thrown into the colon and here abnormal putrifaction and gas formation might take place, and thus, may produce an irritated spastic, or an atonic colon.

The colon is commonly described as being divided into the following portions; cecum, ascending colon, hepatic flexure, transverse colon, splenic flexure, descending colon, sigmoid, and rectum. The sigmoid is further divided into an ileac and pelvic colon. The rectosigmoid is held by most authorities to be of definite significance in most cases of intestinal stasis. It is the shortest part of the colon. The rectosigmoid is the anatomic name applied to that definite portion of the large bowel which consists of the last 5 cm. of the pelvic colon above and the first 5 cm. of the rectum below. At this point where the sigmoid joins the rectum from the left side, there is a sharp angulation as the peritoneum covered colon merges into the retro-peritoneal portion of the pelvis.

The narrowing of the bowel at this point is not the only peculiarity of the anastomosis; there is a distinct difference in the mucous membrane of the two divisions of the large bowel, that of the sigmoid being thrown into rugae and appearing distinct from the rectal mucosa, as the gastric mucosa is distinct from the duodenal mucosa. There is no change in epithelium but there is a definite increase in blood supply. (77)

Examined from the outside the rectosigmoid discloses prominent features of identification; 1. absence of mesentery, 2. the longitudinal muscle bands of the sigmoid spread out, making a complete longitudinal layer for the rectum, 3. the superior hemorrhoidal artery divides into right and left branches at the origin of the rectum, and 4. the absence of epiploic tags, which are found on the sigmoid to its end.

It is the rectosigmoid that is generally conceded to possess the mechanism whereby the fecal current is retarded or stopped so that normally the rectum is always empty. O'Beirne, as early as 1833 (77) commented on "an exceedingly tight narrow neck or contraction" which marks this sigmoid-rectal junction. It has not been definitely proven that this junction possesses a definite sphincteric mechanism, despite frequent

assertions claiming such. W. J. Mayo (63) reported that Reeves in 1917, in disecting out the rectum and rectosigmoid from forty-six cadavers, found a terminal constriction present in eighty percent. More recently (1927), Martin and Burden (62) from observations of thirty one specimens, inconsideration of sphincteric action of the rectosigmoid, concluded that "as a rule the sigmoid has a well developed musculature exhibiting no local increment of circular fibers to suggest an anatomical sphincter, nor is there a perceptible narrowing of the rectosigmoid".

Spalteholz (88) gives the extent of the rectum as being from the sigmoid through the inferior wall of the small pelvis to the inferior opening, the anus. Although the anal canal is often considered as being included as part of the rectum it is derived from the proctodeum (epiblastic infold), is lined with pavement epithilium and has no mucous membrane. The anal canal is about 3 cm. long, beginning where the rectum penetrated the floor of the pelvis, at the level of the levator ani muscles, and has the apex of the prostate directly in front of it and the tip of the coccyx behind and a little above. The canal is incased by the external and internal anal sphincter muscles

and at its upper limit by the levator ani muscles.

The rectum measures from 12.5 to 15 cm. and increases in diameter from above downward. Functionally an anatomically the rectum is readily divided by the plica transversalis recti (the inferior valves of Houston) into two portions. The upper portion is partially clothed by peritoneum on the anterior surface, forming in the male the retrovesical pouch which reaches within 7.5 cm. of the anus, and in the female the retrouterine pouch, or culdesac of Douglas, which is somewhat more accessible to the examining finger. From each side in both sexes the peritoneum is deflected from the front of the rectum onto the posterior wall of the pelvis, thus forming the pararectal fossa. In absence of sphincteric action of the rectosigmoid, it is probable that this upper portion of the rectum serves as a reservoir; it is capable of freely distending into the pelvic cavity by encroachment on the pararectal fossa. (77)

The lower extraperitoneal portion generally is considered the ampulla of the rectum, a term that Paterson (72) considered a misnomer since it occupies a more restricted and confined situation and except in cases of marked constipation rarely contains fecal

matter. It is incased in a dense layer of extra-peritoneal tissue, lies in rectal canal, bound by a layer of pelvic fascia which incloses it; above and in front is the prostate gland and seminal vesicles, or the vagina. Behind and below the pelvic fascia covers the coccyx and anococygeal body, and, on each side the levator ani muscles.

IV. PHYSIOLOGY

As stated previously, no attempt is made in this paper to present general or detailed physiological facts concerning the gastro-intestinal tract. The reader is referred to a text on that subject. I will attempt only to relate some of the most recent attitudes on various fundamental concepts concerning the physiology of the intestinal tract, and more particularly the colon, with special consideration of the pathologic physiology of intestinal stasis.

A. Stomach

The upper part of the stomach is a thin walled sac in which food lies quietly much as it does in the crop of a bird. There is almost no peristaltic movement in this region, and the food drops very slowly and largely by force of gravity into the muscular mill in the lower one third of the stomach. The statement "on an empty stomach" is of course a false one, the stomach is never empty. (37) Some gastric juice is always present. This is 98% water according to Hawk. (40) Gastric juice is largely secreted in the upper two-thirds of the stomach and flows down over the food to be mixed with it. The juice is at first made to flow by nervous stimulation over the vagus,

and later by stimuli arising from the presence of food in the stomach. (2)

There is practically no absorption from the stomach and it merely starts digestion which is done largely by the small intestine. A person can live without a stomach but he must have at least one third of the small bowel. As long as food remains in the stomach waves continue to pass over the lower half, chiefly toward the pars pylorica, kneeding and mixing the food. Occassionally when the stomach is full, or when the person is very tired, or nervous, or there is some disease along the gastro-intestinal tract shallow ripples will run backwards, producing pyrosis, belching, regurgitation, and discomfort in the lower thorax. Further observations on animals by Alvarez (3) have shown that there are many ways in which waves can travel over the stomach and he believes some of the more unusual forms of activity cause discomfort just as similar abnormalities in conduction in the heart give rise to distressing sensations.

When liquids enter the stomach they tend to run rapidly through the pylorus and on down into the bowel. Since one function of the stomach is to warm food and remove from it all those properties which might cause it to be too irritating to the highly sensitive bowel,

it sometines happens that when a cold glass of milk is gulped down too hastily it runs on into the small bowel and will cause colicky sensations of distress. A similar condition may exist in a patient with a gastroenterostomy by food pouring too rapidly into the small bowel. (52) So it might be advisable, in this latter case, to have the patient start his meals with some sort of solid food. The most important factor in governing the rate of departure of food from the stomach is fluidity, and not the acid-base relationship proximal or distal to the pylorus as was commonly held. (4) Solid or lumpy foods may remain in the stomach for hours. Many investigators today feel that increase activity of the small gut reflexly causes closing of the pyloric sphincter so that no more food is passed out until the small bowel is ready to handle it.

Of course gastric digestion depends upon the glands of the stomach secreting pepsin and its activator, hydrochloric acid. Pavlov showed that drinking large amounts of water increased gastric secretion and also gastric acid. (19) Thus, by inference, such a procedure might tend to produce hyperacidity or make such more severe--if not in the healthy stomach possibly in

the subnormally functioning organ. Kellogg (55) although quite generally opposed today, was unfavorable to drinking very large amounts of water and stated that possibly even broths and soups should be avoided in certain cases of hyper and hypo gastric secretion. At the time of publication of his work in 1903 he called the drinking of large amounts of water "misleading and dangerous". This subject will be discussed more fully elsewhere.

Because of the tremendously important part digestive juice plays in digestion, the fathers of gastroenterology naturally expected to find that much indigestion is due to the inability of the stomach to secrete one or both of these substances, but actually the analysis of gastric secretions has proved to be of little value in the study of "functional dyspepsia". Daily persons are found who complain most, and who, when studied, are found to have normal gastric acid. Also, apparently normal subjects who have never had gastric complaints or related symptoms are found to have no acid. Furthermore, rarely does the giving of hydrochloric acid to the patient with low or no gastric acid relieve the condition or complaints. The one condition which

hydrochloric acid does sometimes relieve spectacularly is the looseness of the bowels which, in some cases of achlorhydria awakens the patient at five or six in the morning. (2)

The impression of most writers is that pepsin is present in such amounts that little can be hoped by giving more. Partly because of inaccurate methods of measuring peptic activity and partly because most are interested in only gastric acid little is known about the ways in which pepsin varies in health and disease.(2)

B. Duodenum, Jejunum, and Ileum

The duodenum received its name from the ancient Latin because of its length being twelve inches--duode'ne meaning twelve. The duodenum in its first two inches is thinned walled and poorly muscled. Perhaps this is the reason food tends to stagnate in it, and hence the "cap" is seen when filled with barium. This portion of the duodenum is further important in diagnosis as ulceration is so common here. (2) Kellogg (52) in his recent excellent and very inclusive book on the duodenum states that constipation is frequently but not uniformly present in duodenal injuries. It may be at first due to contusion of this portion of the small intestine and later to peritonitis. He points

out that although it is afforded relative protection from trauma by its position, its limited mobility and close relation to the spine are factors which cause an injury reaching it to be more dangerous. Any blow, kick, or force which would compress the duodenum against the spine or drag some of its fixed points at the superior or inferior angles, is usually responsible. This injury is eight to one more common in males. He collected, up to 1933, 169 cases from the literature.

The jejunum was so named by the Greeks, the word meaning empty. It is so irratable that the food quickly is pushed through it into the ileum, (the"crooked bowel"), and as a result is always poorly outlined in roentgenograms of a barium meal progress.

It is the digestive ferment erepsin that aids in the final splitting of the protein molecule. An insufficient secretion of this may be responsible for some indigestions. For a long time it was thought that the mucous membrane of the bowel would not let undigested protein pass through into the blood stream, but it is known now that often such material does pass through. (3) (75) Hence, by getting into the lacteals it goes directly into the blood stream by way of the thoracic lymph duct and ~~so escapes~~ the detoxification action

of the liver. It is entirely possible that such may be the case for more disease, and especially food allergies, than is now ascribed. The entire field of intestinal absorption, important as it is, is almost unexplored. Recent work which I have found concerning this field is listed elsewhere in this paper.

1. Length of the Bowel in Relation to Types of Food Eaten

Alvarez (2) has given a very practical and interesting account of this topic. Most textbooks state that the small bowel is twenty to twenty-six feet long. This is the condition found in the cadaver however after the muscle of the gut has lost its tone and has become stretched. Actually, recent measurements made on living subjects, with a cord running from mouth to anus, show that it is only from six to ten feet long. It is strongly suspected that the reason why some thin frail persons cannot digest much roughage is that they have an unusually short, carniverous type of bowel.

In the animal kingdom the complexity and length of the digestive tract appears to depend largely upon the amount of grass, leaves, and seeds eaten. A goat can eat the paper off a tin can and digest it because it has a bowel thirty times its body length, and a

big cecum in which food can be kept for ten days or longer. The giraffe which lives on the tough branches of trees, has an intestine one hundred times its body length, while a dog or cat which lives on easily digested meat has a bowel only three or four times its body length. Apparently man with his very short digestive tract was intended to be carniverous. Actually prehistoric man is known to have been a hunter, fisherman and herdsman for untold thousands of years before he learned to live on products of the soil. As some might say, if the Designer of the Universe had intended for us to eat the foods of a rabbit he would have given us that type of a bowel. The full cecum of the rabbit, or the ceropitheccus monkey's stomach which lives on bamboo shoots, makesup one third the weight of the animal. Or perhaps if we had lived on such foods as long as the goat, giraffe, rabbit, or monkey we would have a digestive tract capable of handling such foods. Such facts may well be kept in mind when one thinks in terms of the bulk of a diet relative to intestinal stasis and other disturbances of the gastro-intestinal tract. It is probable that therapy should be at least partially governed by such principles.

2. Why Food Goes Down the Bowel

The bowel has two main types of activity; one, the rhythmic segmenting or swaying movements which churn the intestinal contents and rubs them over the absorbing surfaces of the mucous membrane, and the other the traveling waves which from time to time rush down the gut. (47) Howell (47) gives the classical description of the longitudinal running waves by describing a wave of relaxation just preceding the wave of contraction. This phenomenon was first described by Bayliss and Starling in 1899 and they spoke of it as the "law of the intestine"; it is also described under the name of "myenteric reflex". Many other more recent investigators deny this preceding wave of relaxation. According to Alvarez (3) this downward movement is caused by the more irritable, more active, and more responsiveness to the stimulus of material in the lumen in the upper part of the bowel which gradually decreases terminally. He calls it a gradient of muscular force. By the lower parts of the bowel becoming irritated until it becomes more active than the above the gradient of force is increased beyond that of above and reverse peristolsis, nausea, vomiting and a multiplicity of other symptoms might result. Constipation headaches might well be one

of the symptoms--from pressure and irritation rather than from auto-absorption of toxins. This reversal of gradients serves as a protective mechanism in that irritation distal tends to retard or stop the passage of food above. Many have shown that distention of the colon delays emptying time of the stomach.

A fact to be born in mind by physicians is that it is easier to cause vomiting by irritation of the intestine than the stomach, and so, most efforts to avoid irritation to the stomach by coating irritating drugs, with salol for instance, so that they will pass untouched into the small bowel, are unjustified, irrational, and unnecesaary. Irritating laxatives, therefore, may be entirely undesirable at times. And it is understood why the habitual laxative taker is apt to lose appetite and have impaired digestion because of the tendency toward reversed gradients. It is in this way perhaps that certain drugs, nervousness and fatigue are able to upset the digestion. The gradient can be reversed by injecting irritating substances into the rectum which tend to produce nausea. Some sensitive persons are nauseated by enemas. Vomiting is important because it may be a result of complications of constipation. Phenobarbital is very good to decrease

the irritation to the vomiting center in the brain, which gives rise to vomiting from a multiple of causes other than irritation of the gastro-intestinal tract. However, to overcome a process of reversed gradients either the irritability of the bowel above must be increased, the lower bowel irritability decreased, or a combination of both. As yet no drug will do this. Gradient is reversed in some pregnant animals. (2)

C. Colon

1. Absorption

The main function of the colon appears to be that of water absorption. It allows practically only water to pass thru the mucosa into the blood stream, (1)(45) however small amounts of dextrose and salt are also absorbed. (77) It is well agreed today that any amount of dextrose absorbed by the colon is practically nil, and as a result any attempt to give nourishment by rectum is impractical (1)(9)(45)(65)(77) unless some of the solution is forced back through the ileo-cecal sphincter, which is a harmful procedure. (43)(77)(65) Furthermore, drugs when given per rectum must be administered in doses twice that when given orally. The small absorptive power of the colon is responsible for the fact that

gas tends to accumulate here. In the small bowel much of the gas that is formed there or that is introduced with the food is passed into the blood stream and excreted by the lungs, but the colon mechanism is much less efficient. At all times nitrogen, which represents the unabsorbable remainder of swallowed air, must be expelled through the anus. (3)(77)

Because of the fluidity of the contents of the lower ileum and the cecum bacteria find conditions most favorable for heavy growth. The upper part of the bowel is rendered comparatively sterile or the bacteria inactive by the gastric acid. Also the ileum and cecum are less irritable and food is permitted to remain for longer periods. The abundance of bacteria in these locations probably explains why there is found here the greatest lymphatic deposits, serving as a protective barrier, of any region of the digestive tract. In the distal colon the feces are so dry that bacterial growth is greatly retarded and most of the bacteria are dead.

2. Secretion and Excretion

Mucus is the chief secretion of the colon. It acts as a lubricant to the feces and protects the mucosa, but it is believed to possess no bactericidal power probably serving more as a mechanical barrier.(9)

Larson (57) has found an increase of mucus at defication and that only the stronger cathartics produce copious secretions of mucus. The process does not seem to be a nerve reflex involving the goblet cells, but rather results from stimulation provided by movements of both the mucosa and the remainder of the bowel which takes place continually with the process of defication. Further evidence is supplied by the fact that stimulation of the motor mechanisms results in a stimulation of secretory mechanisms. (57)

It is common knowledge that the colon excretes certain heavy metals, of which calcium is probably the most important. Others are magnesium, iron and phosphorus. Under normal conditions the amount of such excretion is negligible. Also the fact that ulceration of the large bowel is so common in mercury poisoning has led to the belief that this metal is also excreted partially by this route. Bargen, et al, (9) found this to be true, and also that aluminum and bismuth were found in small amounts in colon excretion after having been absorbed from the small bowel above.

3. Motility

The colon is normally a rather insensitive sluggish organ and only occassionally shows evidence of a wave

passing over it, and at such times it is usually shortly after a meal or at defication. (3)(49)(71)

In 1932, Larson, (57) working with trained cecostomized dogs carefully inserted balloons into the colon and was able to make tracings of the large bowel activity under practically normal and under abnormal conditions (by use of purgatives, etc.). These dogs were trained to lie quietly for periods as long as 400 minutes. He found that the colon normally is practically quiescent, and active only when stimulated, which is at varience with most investigators. When movements took place they consisted of three types; 1. large tonus waves at the rate of six to eight per hour, 2. small tonus waves surmounting the large waves at the rate of five to six per four minutes, and 3. short rapid contractions at the rate of eight to ten per minute and superimposed on the small tonus waves. The latter were found only in the cecum and probably produced churning present there. Although waves seemed to travel analward in many instances, they could not be traced from one end of the colon to the other. Usually the whole organ contracted systolically as a unit.

Regardless of Larson's excellent work, many investigators have reported the so called "mass movements" of barium in the colon observed by fluoroscope. (4)(49)(71) The fecal material usually runs together in a sausage-like mass which is slowly but steadily pushed into the rectum. These mass movements probably occur two or three times daily. In those who regularly have a bowel movement before breakfast it is probably the exercise of getting up and dressing rather than the so called "gastro-colic" reflex which brings on this colonic peristolsis. (71) Only when the colon contents are carried into the rectum, which is normally empty, is the reflex desire to deficate brought about, however. If this urge is ignored the material in the rectum will sometimes be moved back into the mid-colon. (4)

In some animals reverse waves of peristolsis are normally seen in the right one third of the colon. Such movements have been described in man but Alvarez (4) has never seen them and concludes that they are so rare and so unusual that they are without significance.

Observations on cats and dogs give the impression that the muscle of the colon is powerful enough for its purpose of moving its contents, and that when it does

not function it is not because it is weak or atonic, but because the normal stimulus is lacking, or because there is failure of coordination, or a blocking or inhibiting influence is arising in a hypertonic rectum. In many cases of constipation the failure of proper relaxation in the rectum may be due to a spread of tonus from the tense voluntary muscles around the perineum, to influences coming down the hypogastric nerves, or to inflammatory processes of the anal ring. (77)

Experiments show that in the presence of diarrhea many irritations, such as from purgatives, will cause the normally sluggish and insensitive colon to become much more highly irritable and abnormally susceptible to inhibitory influences. Some studies indicate that the sigmoid is one of the more irritable parts of the colon.

Pearcy and Van Liere (73) were able to obtain not only hunger contractions in dogs by distention of the colon, but also cardiovascular respiratory reflexes consisting of what looked to them like auricular extrasystole and auricular flutter. More recently however, Monroe and Emery (66) studied the emptying time of the stomach by irritation of the colon with turpentine.

Their results indicate that the emptying time was not particularly influenced; however there was no involvement of the peritoneum in their experiments, so it is possible that the difference in results from other investigators may be due to such a factor.

Rankin (77) reports work done by French investigators, Surmont and Dubus, in 1912, in which conditions were reversed. They applied stimuli to the pre-pyloric and duodenal regions in dogs and cats and noted the effects on the colon. In some cases no reaction whatsoever was elicitated, but in many of them contraction waves were recorded in the colon within one minute. They explained this as due to reflex, possibly related to the so called "gastro-colic" reflex, and not to peristoltic waves passing down the bowel as there was enough time for this to take place.

The rectum appears to have a high degree of automaticity, so much that if serious lesions of the spinal are present rectal incontenance or inability to defi^{9}cate are less common than the corresponding disturbances in the functions of the bladder. Dogs have been kept alive for years with the spinal cord

either transected or destroyed from the seventh cervical segment caudad. Rather prompt recovery was often noted in return of normal defication. The most severe disturbances of defication however are produced usually by destruction of afferent nerves from the rectal region because the animal cannot take cognizance of the fact that the rectum is full and there is nothing to start up the chain of reflexes that normally brings about defication. (77)

One of the peculiar properties of the rectum is its sensitiveness to slight increase of pressure. Even changes from 2 to 3 mm. of mercury could be perceived by persons upon whom Zimmermann in 1909 experimented, and a rise from 20 to 60 mm. of mercury caused distress. Anesthesists have long known that forcible distention of the anal sphincter will have prompt and striking effects on respiration, and, similarly, the distention of the rectum with a balloon will interfere greatly with mental processes. In certain highly sensitive persons distention of the rectum will give rise to symptoms similar to those complained of by patients who believe themselves to be suffering from auto-intoxication. (77)

One of the most interesting bits of striated muscle in the body is that which makes up the external anal sphincter. When separated from its nerve supply it does not degenerate as do other voluntary muscles. (30) It retains its responsiveness to faradic current, and it even regains much of the tonus that it loses immediately after operation. It seems also that it is largely immune to the action of curare, and after transection of the spinal cord it contracts rhythymically. In man the most important nerve centers for anal sphincter regulation appear to be in the third and fourth sacral segments of the spinal cord. Some tonic influences also come from the brain. (77)

Reflex control and reflex stimulation of the colon will be discussed under separate heading.

4. Coloptosis

The general horse-shoe shape of the colon is of course well known. Normally it begins at the right ileac fossa where the ileo-cecal junction is located and terminates at the sigmoid colon in the left ileac fossa. It is also common knowledge that the position and shape of the various portions of the colon may vary greatly in normal persons. Today it is generally held that the shape and location of the colon, per se, has

very little and usually no influence upon intestinal stasis, even in so called abnormally placed colons.

Earlier clinicians and experimentors gave much more importance to coloptosis than more recent investigators. The x-ray and fluoroscope have helped greatly to remove many misconceptions concerning the gastro-intestinal tract. As late as 1916, Grant (36) stated that ptosis of all or any part of the colon is nearly always accompanied by constipation and frequently fecal impaction because of the weakened condition of the intestinal and abdominal musculature. (33) He gives no clinical proof or experimental evidence, and offers no references however. Lochart-Mummary (59) in his book in 1923 finds it doubtful if any serious obstruction of the bowel lumen results from coloptosis unless complicated by adhesions. Both he and Hurst (49), after x-ray studies of enteroptosis did not find delay in passage of feces past the flexures.

Moody (69) in 1929 has probably summed up this subject as well as anyone in recent years. After careful statistical study of large numbers of students in universities he has concluded that the diagnosis of enteroptosis, gastroptosis, or coloptosis is seldom if ever justified, because the position of the viscera

does not produce abnormal symptoms. However Aynesworth (7) as late as 1929 noted that both the cecum and ascending colon of 80% of all persons are securely attached to the posterior abdominal wall, and that in 92% there is very little lateral mobility. From these findings he evolved the opinion that any deviation from this relatively fixed position might cause deleterious changes in function. Based on such observations almost all manner of intestinal diseases have been attributed to greater mobility of the colon, and many of them were said to have been cured by colopexy of one type or another. (92)(15)(46) Rankin (77) definitely disagrees with these contentions. He reports that in his experience almost every type of mobility has been found. He doubts, after following a fairly large number of these patients, if mobile colon is of much significance. He points out that most all such patients have a generally weakened musculature and are run-down and nervously fatigued. He urges that treatment be directed toward remedying these conditions rather than resorting to surgery as all the symptoms which these patients present usually can be explained on the basis of chronic nervous exhaustion. His surgical attempts at cure were on the whole discouraging he relates, and only rarely

was the patient releived more than temporarily.

D. The Biliary Tract and Gallbladder

The chief function of the liver in aiding the digestion of food directly is its formation of certain salts and cholosterin of the bile which aids in preparation of fats for absorption. The gallbladder serves digestion chiefly by concentrating the bile and liberating it when needed, and especially when fat meals are eaten. Both the gallbladder and liver possess the ability to remove bacteria from the blood stream, and excrete them in the bile. Unfortunately they occassionally become diseased in performing this function. It is now understood how blood stream infections from the tonsils, teeth, sinuses, and other focal areas can eventually contribute to a cholecystitis and appendicitis. (2)

Galapeaux, et al, (35) point out various investigators have differed as to their conclusions concerning the action of bile on the colon, some claiming an increase in peristolsis and some a decrease. In their extensive laboratory studies on carefully trained cecostomized dogs, they found that injection of dogs gallbladder bile into the colon was followed by a marked depression in colon activity lasting from

fifty to one hundred minutes. But, in all cases into which bile was injected into the colon defication followed within a few minutes and tenesmus was usually minifested. This may show that the urge and the act of defication are usually associated with inhibition of colonic activity so that voluntary muscles can more easily propel material through the gut. Relative to the use of bile as a drug for relief of constipation Hurst (48) reports a recent medication consisting of an extract of bile, an extract of the intestine with lactic acid ferments, and 0.5 gram of agar-agar, none of which he believes can have the least effect on the bowel.

E. Nerves of the Digestive Tract

One of the most important facts to remember in this connection is that the digestive tract is highly autonomous; that is, it contains within itself all the mechanisms necessary to carry on digestion and to maintain life. In animals if one cuts both vagi coming from the brain and the splanchnic nerves from the dorsal cord region, some of the animals will die of diarrhea and inanition, but others will recover from the operation and will live on, apparently in good health. (47)(2) Many physicians have had the idea that

it is the nerves to the intestine that regulates every detail of direction and control as well as motor power supply to the gut. This is not true, however nervous indigestion is certainly possible and is a disease entity as every physician knows.

Injury to local nervous complexes in the gut wall is probably more harmful than injury to the nerves between the bowel and the brain. Such injury to local nerves might lead to production of conflicts between the activities of different parts of the bowel, with resultant colic. It might cause some failures of conduction along the bowel which surgeons refer to as dynamic ileus, and it might be an agent in producing huge dilated colons seen in cases of Hirschsprung's disease. (32)(2)(76)

1. The Vagi

The principle nerves to the digestive tract are the two vagi. The word vagus in Latin means "wandering", and the vagi are truely such. They "wander" from the brain down through the thorax and on the stomach divide into many branches supplying most of the abdominal viscera. Some investigators (88)(47) claim that the vagi innervation stops at the ileo-cecal valve. Kuntz and others find that in man vagus fibers

reach the descending colon. (2) Below this the corresponding type of innervation comes from the parasympathetic sacral nerves. It has been stated in textbooks (47) that stimulation of the vagus nerve causes contraction of the stomach and bowel. This Alvarez (2) says is only partially true. The response varies greatly with the condition of the stomach and bowel and with different types of stimuli. When the stomach and bowel are contracting and the vagi are stimulated these viscera tend to relax, and when they are relaxed and the vagi stimulated they tend to contract.

In main, the effects from cutting the vagi are that the gut becomes hyperactive and severe diarrhea often results. Thus it is that the vagi act with a "break-like" effect. So too great a vagus stimulation may be concerned in more cases of constipation than is known, probably a spastic type of constipation.

The vagi do not appear to carry any sensory fibers but it is probable that they do. It has been shown many times that the vagi have much to do with the complicated mechanism of vomiting. (47) Pain in drinking ice water is supposed to be due to the spread of stimuli up the vagus to the brain and out along

the fifth nerve. Occassionally also pain in the stomach will be associated with pain around the ear where the skin is supplied by the vagus nerve. (2)

Many theories have been advanced in the past concerning parasympathetic and sympathetic unbalance, "vagotonia and sympathectonia". Recently a vast amount of work has been done both in this country and abroad on this relationship, particularly with relationship to acetylcholine compounds (the parasympathetic mediator) and adrenine (the sympathetic mediator). Cannon and Rosenblueth (20) in their excellent and comprehensive work on this subject in 1937 give detailed consideration of the present knowledge. This subject is discussed at length under the section of this paper devoted to hormonal influences.

2. The Splanchnic Nerves

The main effect of stimulation of the splanchnics is an inhibatory one, tending generally to release the tonus of the bowel. Possibly the preoperative fright or the trauma of surgery itself may be responsible for postoperative paralysis. It is possible also that a variable amount of splanchnic stimulation comes from pain anywhere in the body, discomfort, and worry as well as fear and trauma.

Sympathetic nerve supply to the colon travels by way of the rami from the lumbar cord to the inferior mesenteric ganglia and from there by way of the hypogastric nerves to the pelvic plexus. (88) This arrangement varies markedly in different animals and in male and female. (24)(2) Crile (24) has done a great deal of research on various animals and has shown remarkable similarity in the abundance of the sympathetic innervation in different species of animals whose inherent nervous energy is similar. Much work has been done in studying the effects of sympathectomy both on animals and man in attempts to relieve not only some forms of constipation and megacolon but perhaps also mucous colitis and other painful neuroses of intestinal origin. (94)(31)(24)(32)

3. The Intrinsic Nerves

There are two ganglionated nervous plexuses in the wall of the digestive tract; one, Auerbach's plexus, and the other, Meissner's plexus. Auerbach's plexus is found between the two main coats of muscle and probably has to do with the conduction of waves along the bowel, acting as a correlator of one section with the other, and serves also as a distributing network of the stimuli reaching the gut by way

of the vagi and splanchnics. Meissner's plexus probably serves to correlate the secretory activities of one part of the mucous membrane of the digestive tract with another. Also, through its connections with Auerbach's plexus, it is able to correlate the activity of the intestinal muscle in one part with the work it has to do. (2)(59)(77)

F. Reflex Control of the Intestine

The purging effect of strong emotions has been recognized for centuries. Sullivan (89) in his recent article reviews the literature on this subject and points out that a case of emotional diarrhea might easily be suspected of organic disease, so a causative emotional upset should be looked for. He reports the history of ulcers of emotional origin. Sydenham in 1682 wrote "Hysteria on the stomach will create continued vomiting; on the bowels diarrhea".

1. The Ileo-cecal Reflex

The cecum is quiet probably only when the ileo-cecal sphincter is relaxed, at which time the ileal contents are being forcibly expelled into the cecum.(77) The purpose of the to-and-fro movements of the cecum is no doubt to aid absorption and assimilation.

Alvarez (3) stated that the functions of the ileo-cecal sphincter is to prevent the reflux of foul bacterial laden contents of the colon, where absorption is slight, into the ileum, where absorption is good, and, to prevent too rapid passage of the bowel content through the last segment of the small intestine.

The ileo-cecal sphincter is subject to reflexes such as the "gastro-colic" or feeding reflex, and Hinrichsen and Ivy (44) found that stimulation of the pyloric sphincter resulted in contraction of the ileo-cecal structure; likewise distention of the stomach, duodenum, ileum, or colon resulted in a similar action. After a very large amount of detailed experimentation these investigators concluded that there is just as true a sphincter at the ileo-cecal junction as there is at the pylorus and stands in the same relation to the colon and small bowel as the pyloric sphincter to the duodenum and stomach.

2. The "Gastro-colic" or Feeding Reflex

Among the reflexes that Larson (57) was able to obtain in his experiments was the "gastro-colic" reflex from feeding a dog which had been fasting sixteen hours. The isolated colon responded with large strong contractions lasting fifteen to twenty minutes and

involving the distal more than the proximal colon. It was found that during infection when the dog was fed the reflex was not obtainable. The reflexes were carried through the mesenteric nerves as the response was too rapid for blood stream hormonal effects. He also found definite relaxation of the cecum a few minutes after feeding which allows for the ileum to empty.

Recently however, Slive and Fogelson (82) concluded from their studies on dogs concerning motor activity of the colon that there is no such thing as a "gastro-colic" reflex. They found that when meals were given by stomach tube that peristolsis was neither initiated nor augmented in the cecum, ascending, or transverse colon. When, however, the same meals were given by mouth a marked increase in the rate of peristolsis was seen in the colon adjacent to the cecum in two minutes, and longer sustained contractions were found in the transverse colon. They choose to call this a "feeding" or "appetite" reflex, which is probably more descriptive.

3. Defication

James O'Breine published in 1833 his "New Views of the Process of Defication", which still forms the

foundation of our knowledge on the subject. Cannon in 1902 described the process by aid of x-ray by watching a cat. (42) The process has been studied many times since in man by x-ray and fluoroscope. These studies in man have shown: 1. marked depression of the diaphragm which forces the bowel downward and forces the ascending colon to assume a globular form, 2. peristolitic contractions in the cecum and ascending colon which push some of the feces into the transverse colon, and 3. a wave which empties the descending and pelvic colon. (77) The whole colon seems to take part in the act of defication, so that the material moves from the cecum into the mid-portion to take the place of that which has been moved from the mid-portion and voided. In normal defication the right half of the colon is probably never emptied.

The defication reflex may be initiated not only by masses inside the rectum, but also by any masses outside the rectum in the pelvis which may press on the rectum. It is common knowledge today that the rectum in normal persons is always empty. It is the passage of fecal material from above into it that sets up the reflex for defication. The disregarding of the defication reflex will be discussed in the

following topic.

The rectal valves and their function have been studied by various investigators. In general, more recent experimentors contribute considerable importance to these structures. Pennington (74) described them in detail and stated that they have definite functions, according to his experimental studies on both living and dead subjects. He found that the valves function to prevent the feces from crowding down on the anus, that they tend to equalize the pressure of the feces that accumulate in the rectum from time to time, and that they facilitate defication by giving a spiral motion to the bowel content. In support of his views he cited the fact that man is the only animal possessing these valves and that he is the only animal that defecates regularly. Irritants and foreign bodies cause them to become erect and present a sort of a ledge across the bowel, and in some cases are directed upward forming distinct cups or pockets according to plaster casts he observed taken from them. In certain persons they are enlarged and may interfere with normal defication.

There are many interesting points in common between vomiting and defication as Hatcher and Weiss (39) have

pointed out. They both are brought about by combined and coordinated efforts of involuntary and voluntary muscles. Just as a dog assumes a characteristic attitude during defication, he also assumes a peculiar posture in vomiting. There appears to be a center in the medulla for defication close to the one for vomiting, a center which can be stimulated by the presence of even minute amounts of certain drugs.

4. The Value of Habit

With accumulation of fecal material in the distal colon or rectum the muscle fibers gradually become stretched and distended. If this stretching is continued a point will be reached where they gradually begin to decrease in their contractile power, becoming less and less able to exert their muscular force to expell the bowel content. Finally a point will be reached and if maintained sufficiently long the muscle fibers lose their function completely and the bowel dilates, a similar condition to a dilated heart muscle, and the condition might likewise be spoken of as a decompensated portion of the bowel. Thus a vicious cycle is set up, stasis leading to dilation and dilation leading to further stasis.

It is now seen how by habitually ignoring the urge of defication that the defication reflex may be lost. Such neglect may be attributed to ignorance or laziness but probably very often it is due to thwarting of the defication urge advertently at various socially inconvenient times, women being the worse offenders.

Regularity of this habit should be taught with the greatest of care from infancy. Surgeon-Colonel J. G. Pilcher of the British Occupation Forces in India reports that the rarity of constipation among the natives of India is largely due to the fact that the habit of defecating at an early hour in the morning is universally taught. The mothers in India supports the buttox of her infant on the mother's big toes so that it can defecate between her feet. As soon as the child can walk it accompanies her into the jungle at or before sunrise. The results of this teaching is seen in Indian prisons. The moment the dormatories are opened at sunrise every prisoner rushes to the latrine, and by eight A.M. the whole proceeding for two thousand persons is ended and the material is trenched in prison garden. (19)

5. The Value of Position

World War experience with American troops showed marked hygienic advance when closet seats were replaced by holes in the floor and men were required to "squat". Every obstetrician knows that the lithotomy position is best for delivery of a fetus through the pelvis. (19)

Constipation is also unknown to the children of China and Japan owing to the excellent training they receive from birth. When the Oriental child awakes the mother supports its buttox with her hands and holds it erect with its back firmly held against her breast in which position she presses its thighs against its abdomen. Our "civilized" mothers would probably look with disdain upon such a really rational procedure. The American and Continental children are merely left in their cribs to defecate whenever they can. Practically no thought is given to the mechanical muscular advantages which can be derived from the knees flexed on the abdomen. Almost as soon as our children are able to sit up they are usually obliged to use the same toilet stool, or its counterpart, that adults use. Our present day toilet stools could well be lowered several inches so that the person would more nearly simulate the squatting position of the natives of

India, China, Japan, and Africa. This very feature of lowering the height of the toilet stools is now being done by the most modern and progressive manufacturers. (12)

Furthermore, when our children come to school age they often arise too late for them to have leisure to heed the defication urge and go to school without deficating. At school the child, and especially a girl, may be too shy to ask permission to retire, and chronic constipation is almost an unavoidable sequellae. The defication reflex is partially or completely thwarted and by the age of ten or fifteen the child is chronically constipated. Some school teachers are quite opposed to their pupils "leaving the room" during school time and some have actually imposed some nature of punishment for every time the child asks permission to retire. The physician may well be on guard for such a situation existing in the schools of his locality and take proper steps to correct the conditions. (85)

6. Incomplete Defication

Campbell (19) feels that perhaps the greatest menace of all, as far as intestinal stasis is concerned, is imcomplete defication. He says that this error is frequently practiced by persons who are very

particular as to their personal cleanliness in all other matters. In his experience, he relates, it is almost a regular finding that, in cases of lower colon stasis, from one half to one third of the contents that should have been expelled are left behind.

Hertz (42) says that the majority of cases of stasis, so often associated with visceroptosis, is due to weakness of abdominal and pelvic muscles and ptosis of the diaphragm, which render the act of defication inefficient, so that the rectum and pelvic colon are never completely emptied. Weakness or inability of these muscles to exert their muscular power is exactly what is brought about by mal-position of the person during the act of defication, which was discussed just previously.

G. Hormonal Influences

1. General Considerations

As with all other physiological activities of the gastrointestinal tract, hormonal activity is so closely interrelated, and especially with the nervous mechanisms, that it is difficult to discuss this topic separately. Even though a vast amount of study has been done recently, and is being carried on at present, relatively little is definitely known concerning hormonal

activities. An attempt will be made here to discuss briefly only the more common hormones or "hormonoid" substances concerning which definite information is available.

The fact that the secretions of the digestive tract are not all of nervous control was shown by Ivy when he obtained the usual secretion from a part of the stomach transplanted to the abdominal wall, outside the abdominal cavity, after food given was digested and absorbed into the blood stream. (3) This food absorbed into the blood stream probably released gastric stimulating hormones from various endocrine glands.

Internal secretions from some of the ductless glands when deficient, influence the motor and probably the secretory activities of the intestines. Rolleston (19) confirms the work of Hurst (49) that thyroid gland extract given to some women deficient in thyroid secretion may releive their constipation. Brown (16) reported brilliant clinical results in treating constipation in selected cases of hypothyroidism. Pituitary extract under certain conditions acts as a powerful stimulant to intestinal movements. Larson (57)

found that pituitrin injected subcutaneously in his experimental dogs caused great contractions of the colon. The use of pituitrin in treatment of constipation is as yet only in experimental stages. It is known that, in dogs at least, it will at times increase colonic activity but the indications for its use therapeutically for constipation in human patients and the results are as yet uncertain.

2. Acetylcholine and Adrenine

In 1849 Strecher, a German chemist, isolated a platinichloride base from pig bile but had little or no conception of its importance which is indicated by the fact that he did not report further on the subject for thirteen years, 1862, when he discovered the formula and named the substance choline. In the meantime, and shortly thereafter, similar substances were discovered in many other material, such as mustard seed, brain, roots, barks, the seeds of many plants, and in practically all organs of the body. However, soon all these similar substances proved to be choline also. (17) As work progressed it became obvious that the chemical had a very wide distribution.

Study was greatly facilitated, especially therapeutically, by the synthesis of the chemical by Wurz in 1867. This also made possible the synthesis of choline compounds and derivatives. The importance of this is that, while choline has a therapeutic action, it is weak and evanescent compared to the powerful actions exhibited by many of its derivatives. (17) Thus, synthesis opened the way for therapeutic experimentation with choline and also the vast number of derivatives and compounds based on choline.

In 1911, Hunt and Traveau reported a number of synthetic choline derivatives, and in particular acetylchoine, which was reported as remarkable in that it was one hundred thousand times as active as choline itself. (17) The importance of choline derivatives in the maintainance of gastrointestinal function was first demonstrated by Wieland in 1914, and again by le Heux in 1918. (70) They showed that the isolated gut contained choleine and that the activity of the digestive tract was decreased as the choline was washed out. The action of choline itself was feeble but, when in the bowel it was changed to acetycholine, it was found by them to exert an influence many times greater. It was then thought that the substance was

a peristoltic hormone, but in 1921 Loewi showed that there is a general relationship between acetylcholine and parasympathetic action, and that the drug stimulated the parasympathetic nervous system. (70)

And so it was that very many investigators shared in the long, tedious eighty years of effort which culminated in the work of Sir Henry Dale (27), of London, in 1929. His discovery that acetylcholine could be increased in amount in the body tissues by vagus stimulation, particularly in the bowel musculature, furnished the clue which led to its identification as a body control chemical. It is now generally believed that this natural body chemical, acetylcholine, is formed at the myoneural junctions of the parasympathetic nerves when they are stimulated. It serves as a chemical mediator for distribution of the parasympathetic impulses to the individual cells. This action places it as a physiological antagonist to epinephrine, which is the mediator for the opposed or sympathetic side of the autonomic nervous system.

In 1937, Cannon and Rosenblueth (20) in their excellent and authoritative work on the autonomic system relate the most recent advances in this field. From

their research they concur with practically all recent workers on the subject that, when the sympathetic and parasympathetic autonomic nerves are stimulated a substance is given off at the neuro-muscular junction which has what they term an adrenine-like or acetylcholine-like action--sympathetic stimulation giving the former and of course parasympathetic stimulation the latter. Evidently these investigators are not yet certain that these mediators are actually acetylcholine and epinephrine in pure form. Both these substances are capable of mimicking in the autonomic effecters the changes produced by sympathetic and parasympathetic impulses. So it is now commonly held that it is these chemical substances which exert the influences formerly attributed directly to the nerve impulse.

The action of the acetylcholine-like substance is exactly opposed to the action of the epinephrine-like substance. The administration of acetylcholine, and particularly the administration of some of its derivatives, results in constriction of the bronchioles, slowing of the heart, lowering of the blood pressure, dilatation of peripheral vessels, increase of glandular secretion, and increase tone of smooth muscle,

particularly that of the bladder and bowel. In each instance epinephrine does the opposite; and in the body these two chemicals, when formed in proper amounts are responsible for the fine balance between the two divisions of the autonomic nervous system, which is so essential to health. It is probable that future treatment of spastic and atonic constipation will be more and more by the use of these chemicals when more is known about their actions and more useful and specific derivatives are discovered.

But now, why do such mediator substances produce different effects in different organs, or even different effects in the same organ, as the bowel for instance, under different conditions? To account for this phenomenon Langly in 1905 assumed the presence in the responsive cells of a differentiating receptive substance which would determine whether a single agent, adrenine or acetylcholine would produce contraction or relaxation in a given set of smooth muscles. (20)

Acetylcholine chloride was one of the first forms in which the drug was used in therapy, but its therapeutic value is interfered with because of its rapid distruction in the organism by a tissue and blood esterase. (17) In search for a stable compound

a large number of choline derivatives were synthesized, and attempts made to evaluate them therapeutically followed. Major and Cline (61) in 1932 synthesized acetyl beta methylcholine chloride (mecholyl). To date it has been chiefly used in treatment of a paroxysmal tachycardia and peripheral vascular diseases. Myerson, et al (70) in 1937, after a rather large series of cases with controls, came to the following conclusions concerning the use of "mecholyl"; 1. "mecholyl" increases the tonus of the colon to spacticity and at the same time increases the motility of the colon resulting in increased evacuation rate, and 2. atropine banishes any effects produced by "mecholyl". But they further conclude that clinically the drug is of doubtful value in treatment of atonic colons because of its unpleasant side-reactions such as rise in pulse rate, drop in blood pressure, salivation, rhinorrhea, lacrimation, flushing, and sweating could be eliminated by some subsequent modification drug, it is very possible that it could be used advantagously in the stimulation of the atonic colon.

Burgett and Bardens (17) report a series of cases in which "lentin", a new choline derivative,

spectacularly cured a number of horses with severe fecal impactions. This drug was discovered to expend its action preponderantly on the alimentary canal. It was found to be unusually stable, slowly destroyed in the organism, it is stable in both solid and in solution form, it is thermostable so can be sterilized by boiling, and it is effective orally, all of which are not possessed by choline derivatives generally. However, from the authors' description of the actions of the horses and the apparent effects of the drug on them, it does not seem that undesirable side-reactions have been eliminated. I have been unable to find reports of this drug "lentin" (Merck & Co.) being used on human cases.

H. Effects of Water Drinking

Misconceptions concerning the effects and advisability of taking of fluids before, during, or after meals are common among the laity, and not infrequent among physicians. There has been a great deal of work done on the subject in the past and the rationale of fluid effects on digestion is now on a substantial physiological basis.

Hurst (49) observed that dryness of the colon

is a condition of practically all forms of intestinal stasis and that those who suffer from the condition, and particularly women (25), are notoriously poor water drinkers. Starling, who was one of the early workers in this field, believed that water drinking did not increase the fluidity of the colon, but Campbell and Detwiller (19) disagree and point out that Starling himself said that there is relatively as much moisture at the lower end of the small intestine as there is at the upper end, and then further goes on to state that the moisture is practically the same on both sides of the ileo-cecal valve.

Hawk (41) found that soon after drinking copious amounts of water it can be demonstrated far down in the small intestine. Warm water at body temperature flows through the stomach almost immediately (3) so that if increased fluidity of colon is desired warm water should be drunken and on an empty stomach. (55) Two or three glasses before breakfast will probably do more to cure many cases of constipation than any other one thing. Warm water to many people is distasteful and even nauseating and cold water is then adviseable, it becomes body temperature very soon. (12)(48) Hurst (49) and practically all other

reliable investigators found that if the above procedure is carried out and if there is no obstruction in the small bowel, a condition which would be rare, the moisture in the colon will become pronounced and effective almost without exception. But for serious impaction in the lower bowel it is of course better to first relieve by enema and so getting the moisture where it is needed most.

It has been further pointed out that drinking water before breakfast tends to "wash out" the stomach and possibly also tends to relieve the kidneys by diluting the blood. It was also suggested that drinking of warm water before breakfast was stimulating in that it helped to raise general body temperature which is subnormal in the morning upon arising. (49) Whenever moisture is presented to the absorbing surface of the intestine it is absorbed, and absorption is influenced very little by the amount of body depletion according to Starling. (19) The bowel absorbs and it is the kidneys that regulate the body water content. The small bowel absorbs most of the water, the amount of moisture going on into the colon is probably no more than is added to the intestine by the stomach, pancreas, liver, and bowel itself.

This amounts to about two and one-half quarts of fluid every twenty-four hours normally. (41) While the small intestine absorbs large amounts of water it also secretes so that the amount of fluid at the ileo-cecal valve is quite as much as at the pylorus. On the other hand, the colon only absorbs, and its contents lose water readily while in the cecum and ascending colon, and, before it reaches the descending colon it has acquired the ordinary consistency of the feces. (47)

Hawk (41) concludes from his investigations that the common notion is entirely erroneous that drinking water at meal times, thus diluting the digestive juice, is farmful; he found that water drinking at meal times, even up to a quart, actually stimulated the flow of gastric juice, and further added that drinking water between meals may actually be a glandular waste. He found that digestion and absorption in the small bowel was even better and more complete when an abundance of water is drunk at meal times. Bergeim and Hawk (10) demonstrated further that the moisture of the colon actually decreases, showing a stimulation of the power of absorption. They found, on governed experimental conditions, calculated on a dry basis, that there were twenty-three grams of dry excretion

per day during the preliminary period as against seventeen grams per day for the water period (taking a quart of water with meals). Hence, to insure more moisture reaching the colon in treatment of constipation an increase in the amount of water should be between meals rather than during the meals. But, if the patient wishes to gain weight by greater stimulation to the digestive, absorptive, and assimulative mechanisms, drink much water with the meals.

Campbell and Detwiller (19) report that actual weight gains are recorded in those subjects who took large quantities of water with their meals, and Hawk (41) determined by his experiments that carbohydrate metabolism was enhanced. He went into detail concerning the large percentage of water in the certain body fluids and reported the following; gastric juice 98% water, blood over 90%, intestinal juice 98%, and lymph about 95%. Is it any wonder that digestion, absorption, and assimulation are enhanced by large water intake?

In his conclusions on the subject of water drinking Hawk (41) states that "most people drink too little water" and that "If you are normal, by all means drink all the water you want at meals". He feels

that the bowels can be "flushed" as well as the kidneys. The amount of water one should drink in a day depends upon many factors, such as, vocation, temperature, humidity, body weight, exercise, character of the diet etc. It is quite well agreed now that about six to ten glasses of water or about two quarts, is best for the average man or woman. (8) (28)(41) (55)(19) Probably most benefit can be derived by taking the equivalent of three glasses of fluid at each meal and then any extra desired between meals. Foods of higher water content of course reduce the amount needed. Milk is 87% water, tea and coffee almost 100%.

Priessnitz of Groffenberg, Gernmany, the originator of hydrotherapy, recommended the drinking of twenty to forty glasses of water per day in the so called "water cure". Of course many disease conditions and some strenuous physiological conditions require such large amounts of water. Large quantities are indicated in most all cachexias and diatheses, rheumatism, most fevers, dehydration etc. It has been known for a man weighing 150 pounds to lose eight pounds in three hours of fatiguing tennis on a scorching hot day. (19) Of course practically

all this is water loss and amounts to over four quarts. Similar and greater weight losses are not uncommon following hot football games.

1. Milk Drinking

McLester (64) condems severely the statement that milk is constipating and says that such is slander against a very important food. The only objection to milk, he says, is that the patient who takes it in large quantities is less likely to eat other foods in amounts to give sufficient roughage. It is proper to give a constipated person milk, provided that he obtains from his other foods sufficient cillulose. (64)(45)

It has been shown definitely that fats in a diet are of considerable aid against constipation. (64)(83) Fatty acids even in large amounts, though not over perhaps 225 to 250 grams of fat per day, have a stimulating effect on the mucous membrane, but too much fat will cause a diarrhea or perhaps alternating with spastic constipation. It is now seen how milk with a high cream content does aid in protecting against constipation. (64)

Hosoi, et al (45), state that if it is desired to prevent bowel movements milk should not be given.

The large residue often left in the terminal ileum after taking of milk may account for the fact that milk is not well tolerated by many persons and that it makes them "bilious". This is an important point because milk is often prescribed, and at times nothing else, in order to give the bowel rest. Some are also prone to use milk for diarrheas although it should be one of the first foods withdrawn. It was their experience that milk had a bad effect on many persons with diarrhea who would promptly get well when nothing but a little meat with a little pure starch and sugar was given. There is no significant difference in the effects, digestability or nourishment of boiled and raw milk, a fact which was again recently proven by extensive research on growing children by the U. S. Department of Agriculture. Condense milk was not digested as well as fresh milk. They also found that milk added to other foods does not decrease their digestability.

Campbell and Detwiller (19) suggest that when it is desirable that a patient drink large quantities of milk it will be more easily taken and better tolerated if the patient takes the milk slowly, as sipping through a straw or glass tube. As much

as six quarts per day can usually be tolerated without difficulty, which might otherwise result in formation of harmful curds. They report that after one of their patients had drunk several glasses of milk rather rapidly, a curd, in the form of a rope, was felt in the throat several hours after. Campbell was able to grasp this curd with his fingers and pull it out of the esophagus. Dr. Lawson Tait, famous English surgeon, told Kellogg (55) of a case where he was obliged to remove similar curd masses low down in the intestine. Under very abnormal conditions such curd formation might occur, but I was not able to find any such reports in recent literature.

I. "Auto-intoxication"

Some busy nervous people cannot wait for defecation because they soon feel dopey, stupid, and "poisoned", and so, take a purgative with usual immediate relief. Others never notice such when they become constipated and experience no discomfort or distress at all, but can not wait for nature because of the fear of so called "auto-intoxication" of which they have been so well warned against by those who assume such to be a fact.

This conception has always had a strong hold on the minds of the laymen and physicians because it seemed to be so rational and so obviously true.

It was the "opinion" of most of the earlier "authorities" on the gastro-intestinal tract that intestinal auto-intoxication was true, (54)(13)(19), and this "opinion" is held by many physicians and practically all the laity today. They attribute this condition to be the cause of almost any form of vague complaints, symptoms, or disease condition in almost any organ or system of the body. A number of disease conditions which I found attributed to the results or effects of auto-intoxication are; eye troubles, bad breath, tongue conditions, multiple of kidney disorders, high and low blood pressure, pelvic diseases in women, loss of weight, anorexia, lethargic states, neuritis, mastitis, lymphadenitis, rheumatism, mal-functions of the thyroid gland, arteritis, arterosclerosis, atheromata, psychic and nervous disorders, arthritis etc., etc. It appeared to me from reviewing their writings on this subject that almost any condition which could not be readily explained or whose etiology is unknown, could be or was likely to be caused by intestinal intoxication.

Alvarez (1)(2)(3) insists that thousands of physicians use such a diagnosis largely as a cloak for ignorance. The patient gladly falls in line with the idea because in every magazine, newspaper, and radio, on signs and in circulars, it is told of the terrible results which will follow if he does not take this or that "intestinal bath", or if he fails to buy so and so's "laxative pills", or patented syringe, or parafine oil, yeast, vitamines, sour milk, agar or bran.

Since the publication of the earlier work and writings on intestinal absorption of putrifactive toxins, more recent investigators in this field are more or less regarding auto-intoxication as an improbable supposition. It is possible that auto-intoxication may exist. (1)(75)(40) Highly toxic substances formed outside the body can go through the mucous membrane and poison us. Children have been often severely poisoned and even killed by substances formed in the bowel, but, at these times they suffer from diarrhea, and much evidence has accumulated to show that they are poisoned and killed not so much by chemical toxins as by living bacteria which pass through the intestinal wall into the blood

stream. (2) The passage of bacteria through the intestinal wall of the cecum and terminal ileum into the lymph passages and nodes of the mesentary is much more deleterious to health than the passage of chemical substances. A number of investigators have shown that bacteria are constantly getting through the bowel wall, and after purgation or intestinal upsets this low-grade infection of the lymphatics or blood stream is severe enough to endanger health. (1) This area being the most vulnerable probably accounts for the large amounts of lymphatic structures in this region. Besides bacteria being more apt to pass through a mucosa which has been injured or irritated by purgatives, the bacteria are also enormously increased in numbers and virulence because the fecal material is more liquid. Furthermore, there is more absorption from a liquid feces than from a comparatively dry feces as there is more intimate contact with the absorbing mucosa. (3) So, a patient is less apt to have auto-intoxication when they are constipated, when the feces are dryer. Hurst (48) in his recent (1937) publication on constipation also concurs with these outlined principles in being opposed to the idea of auto-intoxication.

Hawk and Bergein (40) in their recent textbook (1931) on physiological chemistry state that due to bacterial action many more or less toxic compounds from protein materials are formed in the intestine--the large intestine chiefly. This statement no one could refute. But, they further say that because of the absorption of these toxic substances symptoms of general irritability, sleeplessness, anorexia, melancholia, and general mental depression results. Here again we find a group of rather vague symptoms and surely of unknown etiology. These authors give no references, experiments, or qualifications relative to the truth of these statements. "Before anything definite can be known about auto-intoxication researchers must find some substance which is formed in the bowel, which can get unchanged through the mucous membrane, the liver and the lungs (and kidneys); which can be absorbed in amounts sufficient to produce symptoms, and which will produce symptoms ordinarily ascribed to auto-intoxication". (2) Actually, although much research has been done, no such substance has been found.

Powers and Sherwin (75), after extensive experimentation concerning auto-intoxication on both

lower animals and man, proved quite conclusively that the human body is apparently provided with a chemical defense mechanism, nonspecific in character, which is more than adequate for detoxification of the small amounts of putrifactive products normally produced in the human intestine by action of putrifactive bacteria on unabsorbed protein materials. The site of detoxification, according to them, appears to be the liver, but to some extent also the kidneys and gastro-intestinal wall. Amino compounds proved much more toxic, 20 to 100 times, than non-nitrogenous toxins. They were detoxified in the body by splitting off nitrogen. These workers analysed the toxins and found that it was the nitrogenous products phenylethylamine, tyramine, and indolethylamine from the three amino acids phenylalanine, tyrosine, and tryptophane that were the most toxic. These, as well as other toxins were fed to man in doses much greater than found in any obstructive condition, and only then did the above mentioned toxins produce toxic symptoms. The mode and form of the excretion of the toxins were also noted. These toxic symptoms consisted of a feeling of nausea, temporary anorexia, high nervous tension,

sleeplessness, followed usually in a short time by a feeling of impending evil, and always a severe diarrhea. There was a slight elevation of temperature and an increase of pulse rate, with a rise in arterial tension.

There is no question that many persons feel "poisoned" and miserable when they are constipated, but the important point is that the symptoms clear up instantly after bowel movement. When such prompt relief is experienced the sufferer can be sure that there has been no chemical poisoning because in that case relief would come slowly after the poison had been destroyed or excreted in the urine. (2) The symptoms complained of are real and in those patients who get relief immediately after defecation the distress was produced mechanically by distention and pressure on sensative nerve endings in the rectum. (77) Rectums vary in sensativeness so personal differences are concerned with the production or non-production of symptoms of auto-intoxication experimentally.

Fear of auto-intoxication must be dispelled from the patient before he can be convinced to leave his bowel alone. Some will then get prompt relief,

some may go on a vacation and get relief, others may need to be taught proper diet and exercise habits. For those who can gain comfort and relief from no other means they can, if their digestive tract will permit, take some mild cathartic, every two to four days, such as magnesium oxide, hydroxide or citrate, or cascara. Hydrocarbon oils tend to coat food with an oil film and render them indigestable. (5) Two or three glasses of water before breakfast may suffice in some persons. A physiological saline enema, one tablespoon of salt per quart of luke warm water, is often the best means of emptying the colon, and daily use will do no harm. (3) The matter of detailed treatment of constipation is a subject in itself and is in the donfines of this paper only indirectly as digestive functions are altered by changes in physiology.

J. The Feces

It is the popular conception that the feces are made up chiefly of undigested food materials. This is far from true. It is composed chiefly of gastro-intestinal secretions and excretions (notably calcium salts, iron and other metals), cellular elements of the intestinal wall, bacteria, and

(except in cases of diarrhea) only in small part of food residues. (64)(40) Under pathological conditions of course the feces may contain a multiple of materials, such as; blood, pus, mucus, serum, parasites, enteroliths, gall stones, pancreatic calculi, etc.

Hosoi, et al (45), quotes Bischoff and Voit--1879, Muller--1879, Rubner--1879, and Prausnitz--1889 and 1890, that, so long as foods given are completely utilized, the amount of feces will be the same with different diets. Even in starvation a certain amount of feces will be formed. Concentrated foods such as milk, cheese, eggs, meat, and white bread are absorbed almost in toto and therefore leave very little residue. When large amounts of fruits and vegetables are eaten there remains a rather large amount of undigestable cellulose. This undergoes fermentation, and, through absorption of water, gives the bowel content proper bulk. Alvarez and Freedlander (4) in their experiments on human subjects in following the rate of progress of glass beads through the intestinal tract found that not all fecal material passed through the tract at the same rate of speed. The beads taken at one meal, some were passed in the normal time of about thirty

hours, and a few required a week or more. Cannon found, in the cat, that proteins passed through the small intestine slowest, fats faster, and carbohydrates fastest. (45) Work done by Ehrlich has shown that bacterial break-down of proteins and their amino acids (putrifaction) may yield the same end-products as bacterial decomposition of carbohydrates (fermentation). (40)

The little balls of feces of rabbits become so dry that they float on water. The feces of the constipated person floats, whereas if the stools are somewhat loose, much of the material goes to the bottom of the toilet bowel. It has been pointed out that if the patient's bowel contents are passed in hard or very firm masses that he does not have a stricture of the lower colon. (29) In all cases the specific gravity of the feces is so near that of water that one can not consider the cecum or sigmoid flexure as being "weighted down" with excrement. The colon and its contents can be said to float in the abdomen, and the mesentery serves more as guy-ropes than a support. (77)

V. GENERAL CONSIDERATIONS OF CONSTIPATION

Cecil (21) in his recent Text-book of Medicine defines constipation as a disturbance in intestinal function, usually of the colon, which results in delayed or incomplete defecation. Recent medical attitude on functional disorders of the colon defines them as an apparent alteration in secretory, evacuative, and excretory functions. The number of stools in apparently normal persons may vary from one in several days to eighteen or twenty within a period of twenty-four hours. Such cases as spastic ileus (82), mucous colitis, colopathy, nervous diarrhea, and constipation are now designated as functional disorders. (87) Perhaps one of the greatest lessons to be learned from the study of this subject as it is related to intestinal stasis is that the condition is not a disease in itself but merely a manifestation of one or several pathological conditions and therefore should be classified as a symptom. Whereas a single basic cause was formerly sought for, now we seek a multitude of causative factors, and having found them, it appears that too many try to relate them to a single basic source of systemic disturbance.

Constipation is one of the most troublesome complications that the physician has to meet in caring for patients confined to a hospital. To resort to cathartics has come to be recognized as an acknowledgment of defeat; the prolonged use of purgatives (26)(84)(5) or enemas (58)(14)(67)(34)(5) merely postpones the day of reckoning to the day when the patient is no longer under the care of the same physician, and the use of indigestable materials such as bran (81)(5), agar-agar (5), and liquid petrolatum (5) is not without disadvantages. (68) All such measures are losing in popularity and giving place to proper exercise when possible (80)(11), physical therapy (53)(56)(78)(23), and the endeavor to provide the diet with sufficient fluids and adequate bulk in the form of vegetables and fruits, so that the residue left in the bowel after digestion is completed will be sufficient to stimulate periodic evacuation. (50)(95)

The patients who seek medical aid for their constipation usually have tried all manner of propietary preparations--laxatives, oils, purgatives, and perhaps colonic irrigations. These drugs are often as much to blame for their symptoms as the

the actual constipation. The first order for treat- should be to stop every form of medication that the patient is taking for his constipation. A thorough history considering the nervous qualities and abilities of the patient (18), past treatments, diet, and exercise should be t aken. A physician would not attempt to diagnose and treat tonsilitis without first examining the tonsils, and just as surely he should make a rectal examination in all cases of constipation. This is very important to rule out anal and rectal neoplasms which are perhaps the commonest of all gastro-intestinal malignancies. Many a case of constipation is cured by correction of common rectal and anal pathology, hemorrhoids, fissures, etc. At times only a thorough gastro-intestinal study will make the diagnosis of the type and location of the constipation as well as ruling out new growths and other organic conditions. (2)(12)

After the diagnosis is made the next step is to sit down with the patient and discuss in detail the course and nature of the disease. The rationale of the treatment being prescribed should be presented in a clear and convincing manner. (18) The enlighten-

ment of the patient concerning a few fundamental facts concerning the physiology of digestion and elimination with logical proofs of these facts will do much to aid the patient in curing himself. Re-education of the patient as to the necessity of never neglecting a call to stool, to visit the toilet regularly and take plenty of time, drink plenty of water, especially before breakfast, and eat regularly a balanced diet are among the important considerations.

A change of intestinal flora by replacement with bacillus acidophilus has been used to treat some cases of constipation with good success in selected cases. (79)(93)(23) This form of treatment entails a small amount of laboratory equipment and some knowledge of the care for bacterial growth, bacterial counts, and stool examinations. Avitaminosis (38) (96) has also been reported to have resulted in constipation and to have been relieved by vitamin therapy. A puzzling case of obstipation due to mesenteric adenitis, probably tuberculous in origin, was reported by Trimble in 1937. (90) Soper of St. Louis (87) uses and recommends local treatment of a spastic, ulcerated, or infected rectum or sigmoid. Through

the sigmoidoscope he blows into the lower bowel a coating of powder consisting of equal parts of bismuth subcarbonate and calomel, which he says is non-irritating and antiseptic. He reports good results. Clendenning (23) recommends, for spastic conditions, a solution of 50% magnesium sulphate instilled through a catheter into lower colon and the patient instructed to lie on the left side for fifteen minutes. This treatment is to be given daily until the spasm relaxes. Only temporary relief can be obtained by this procedure however, he reports.

VI. CONCLUSIONS

1. Developmentally, anatomically, and physiologically the right and left halves of the colon differ so much that it is virtually a dual organ.

2. Normally the rectum is always empty except at defication when it becomes filled and so initiates the defication urge.

3. The rectosigmoid is thought by most investigators to have definite sphincteric action however this has not been proven.

4. "Ampulla" of the rectum is a mosnomer as it occupies a more restricted and confined situation and only in cases of severe constipation contains feces.

5. The large bowel absorbs little if anything besides water, so attempts to give nourishment per rectum is impractical.

6. Increase of internal rectal pressure, as little as 2 to 3 mm. of mercury, causes in many

persons most of the ill-feelings resulting from constipation, many of which are attributed to auto-intoxication.

7. The external anal sphincter is perhaps the most peculiar and interesting bit of striate muscle in the body.

8. Normally functioning colons have such extreme range of positions and movements that a diagnosis of enteroptosis, gastroptosis, or coloplosis is seldom if ever justified. Surgical attempts to correct such conditions are practically always useless.

9. The digestive tract is very highly autonomous. It contains within itself all the nervous mechanisms necessary to carry on life, and injury to the intestinal wall is probably more harmful than injury to the nerves between the bowel and the brain.

10. The main effect in stimulation of the parasympathetic nerves to the bowel is a "brake-like" action, hyperstimulation possibly leading to a form of spastic constipation. Whereas, the main

effect of stimulation of the sympathetic nerves is generally a release of tonus, possibly leading to atonic constipation. Such emotions as fright, pain, worry, etc. tend toward hyperstimulation of the sympathetic system.

11. There is probably no such thing as a "gastro-colic" reflex, a feeding or appetite reflex is suggested as being proper.

12. The rectal valves are definite structures and have definite and important functions.

13. A regularity of habit of defication is very desirable and should be taught from childhood. Likewise a child should be taught never to fail to heed the urge of defication.

14. Toilet stools probably should be lowered several inches so as to enable the person at defication to more nearly simulate the "squatting" position, hence gaining full use of accessary muscles.

15. Thyroid gland extract administered to some carefully selected cases of hypothyroidism probably

is very useful in increasing muscular tone and activity of the atonic colon.

17. Pituitary extract under certain conditions acts as a powerful stimulant to intestinal movements, but at present its clinical use in therapy of the atonic colon is only in experimental stages, the indications for the use of the drug and the results are not at all certain today.

18. Acetylcholine, the parasympathetic mediator which is formed at the myoneural junctions of the parasympathetic nerves, at present, has no clinical use today in treatment of atonic constipation. The actions of some of its derivatives on the gastro-intestinal tract give the encouragment that a very useful drug from this source may be available in the future if the rather serious side-reactions can be eliminated.

19. Adrenine or the epinephrine-like substance formed at the myoneural junctions of the sympathetic nerves is a sympathetic mediator and an antagonist to the acetylcholine-like substance. As yet no therapeutic use of adrenine in treatment of spastic

-constipation has been reported.

20. In order to increase colon fluidity, drink larger amounts of water between meals. Two or three glasses of water before breakfast on an empty stomach will cure many cases of constipation. The colon fluidity is increased.

21. Drinking large amounts of fluids during meal times is stimulating to digestion, absorption, and assimulation, and the patient will more readily gain weight. The colon fluidity will be decreased however.

22. Milk is not constipating, but conversely, it stimulates the gastro-intestinal tract to activity. Therefore it can be given in constipation provided the patient gets sufficient bulk elsewhere. It is definintely contra-indicated in diarrhea.

23. So called intestinal "auto-intoxication" probably does not exist, and expecially not in constipation.

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