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Chronic ulcerative colitis

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Anatomy of Colon

Full understanding of the colon, its functions in health and in disease cannot be fully appreciated without some knowledge of the basic structure of this organ. The colon is divided into four parts: the ascending, transverse, descending and sigmoid. It has four coats: serous, muscular, areolar and mucous.

The serous coat is derived from the peritoneum and invests the different portions of the large intestine to a variable extent. The cecum is completely covered by the serous membrane, except in about five percent of cases where the upper part of the posterior surface is uncovered. The ascending, descending and iliac parts of the colon are usually covered only in front and at the sides. A variable amount of the posterior surface is uncovered. The transverse colon is almost completely invested, the parts corresponding to the attachment of the greater omentum and transverse mesocolon being alone excepted. The sigmoid colon is entirely surrounded. The rectum is covered above on its anterior surface and sides; below, on its anterior aspect only. The anal canal is entirely devoid of any serous covering. In the course of the colon the peritoneal coat is thrown into a number of small pouches filled with fat. They are most numerous on the transverse colon.

The muscular coat consists of an external longitudinal and an internal circular layer of non-striped muscular fibers.

The longitudinal fibers do not form a continuous layer over the whole surface of the large intestine. In the cecum and colon they are especially collected into three flat longitudinal bands each of about 12 mm. in width; one, the posterior, is placed along the attached border of the intestine; the anterior, the largest, corresponds along the arch of the colon to the attachment of the greater omentum, but is in front in the ascending, descending, and iliac parts of the colon and in the sigmoid colon. The third, or lateral band, is found on the m edial side of the ascending and descending parts of the colon and on the under aspect of the transverse colon. These bands are shorter than the other coats of the intestine and serve to produce the sacculi which are characteristic of the cecum and colon; accordingly, when they are dissected off, the tube can be lengthened and its sacculated character disappears. In the sigmoid colon the longitudinal fibers become more scattered; and, around the rectum they spread out and form a layer, which completely enc ircles this portion of the gut, but is thicker on the anterior and poster or surfaces, where it forms two bands, than on the lateral surfaces.

The circular fibers form a thin layer over the

cecum and colon, being especially accumulated in the intervals between the sacculi; in the rectum they form a thick layer, and in the anal canal they become numerous and constitute the sphincter ani internus.

The mucous membrane in the cecum and colon is pale, smooth, destitute of villi and raised into numerous cescenter ic folds which correspond to the intervals between the sacculi. In the rectum it is thicker, of a darker color, more vascular and connected loosely to the muscular coat.

As in the small intestine, the mucous membrane consists of a muscular layer, the muscularis mucosae; a quantity of retiform tissue in which the vessels ramify; a basement membrane and epithelium which is of the columnar variety and resembles the epithelium which is of the columnar variety and resembles the epithelium found in the small intestine. The mucous membrane of the large intestine presents for examination glands and solitary lymphatic nodules.

The glands of the great intestine are minute tubular prolongations of the mucous membrane arranged perpendicularly, side by side, over its entire surface; they are longer, more numerous, and placed in much closer apposition than those of the small intestine; and they open by minute rounded orifices upon the surface, giving it a cribriform appearance. Each gland is lined by short columnar epithelium and contains numerous goblet cells (1).

The functions of the colon are initiated from two

sources; the extrinsic and intrinsic nerves. First, we shall consider the extrinsic innervation. For a variable distance from its commencement the large intestine is supplied with motor fibers through the vagus. Most usually the vagal innervation terminates within the first half or third of the transverse colon. The rest of the colon, including the rectum, receives its motor innervation through the pelvic nerves from the second, third, and fourth sacral segments.

Inhibitory fibers to the entire colon are derived from the sympathetic. They arise from the lumbar segments of the cord and reach the proximal part of the colon (cecum, ascending and transverse colons) through the interior mesenteric plexus. The fibers to the distal colon (descending, iliac, pelvic colons, and rectum) arise from the second and third lumbar segments. They pass via the lumbar splanchnics to the inferior mesenteric ganglion and thence to the bowel by (a) a number of short strands called the lumbar-colonic nerves (also known as the inferior mesenteric nerves), and (b) the hypogastric nerve. The lumbar-colonic nerves are the axons of cells situated in the inferior mesenteric ganglion. The fibers entering into the formation of the hypogastric nerve pass for the most part without interruption through the latter ganglion. Their cell stations are situated in the hypograstric ganglion.

The post ganglionic fibers pass through the pelvic pl exus to the bowel.

Stimulation of the lumbar-colonic nerves causes relaxation of the distal colon. Learmonth and Markowitz showed that these nerves exert a constant inhibitory action since increased colonic activity follows their section. Garrey found that though in the decerebrate cat the distal colon is inactive when its sympathetic supply is intact, division of the lumbar-colonic nerves caused rhythmical activity and a marked increase in tone. The hypogastric nerve appears to exert a minor inhibitory influence upon the colon since its division causes only a slight increase in the activity of the bowel. Paralyzing the lumbar outflow by a spinal anesthetic has an effect similar to that of nerve section. The inhibitory impulses to the colon arise apparently within the lumbar cord, for if this region has been isolated previously from higher centers by spinal transection, the full augmentor effect upon the colon of sectioning the colonic nerves is obtained.

Section of the pelvic nerves relaxes the wall of the distal colon and the anumal subsequently experiences difficulty in emptying the bowel. The effect of section of the pelvic nerves upon the tone of the colon is particularly well shown if the bowel has been previously in a hypertonic state as a result of division of the sympathetic supply.

Sectio n of the cord above the sacral segments also causes relaxation which indicates that the constant augmentor effect is due to impulses arising in higher centers. A subsidiary augmentor center apparently exists, however, in the sacral cord, for cutting the pelvic nerves some time after spinal transection causes colonic relaxation. That is, the sacral segments acquired control during the time which had elapsed after their isolation from higher centers.

The intrinsic innervation of the bowel is composed of a plexus between the two muscular sheets, the myenteric plexus (Auerbach's). In the submucosa is situated the plexus of Meissner. These two plexuses are connected with one another by nerve filaments which pass between the circular muscular fibers. Auerbach's plexus contains numerous ganglion cells; these are scarce in Meisser's plexus.

The rhythmical contractions - segmenting and pendular - and myogenic in nature, that is, they are dependent solely upon the rhythmical property of the intestinal muscle itself. Furthermore, the contractions of the circular coat of the bowel have been shown by Gunn and Underhill and by Alvarez and Mahoney to continue after it has been stripped from the longitudinal layer, and from the submucosa as well; all ganglion cells are in this way removed.

T he peristaltic contractions, on the contrary, are dependent upon the intrinsic nerve plexuses. But though

carried out through local reflexes in the bowel wall they are readily influenced through the extrinsic nerves, the vagus and sympathetic. The vagus, whose terminals connect with ganglion cells in Auerbach's plexus, augments the movements. The sympathetic is inhibitory (2).

Colitis

Any involvement regional or general of the large intestine above the lower part of the rectum resulting in a sanguineous, a mucosanguineous, a mucopurulent or a mucopurulent-sanguineous exudate, with or without diarrhea due to known or unknown factors, save that of neoplasm, is a colitis. Clinica ly, the corollary follows that a colonic exudate or feces containing blood, mucoblood or pus, or all of them, is due to a colitis when neoplastic disease and perianal, perirectal and localized disturbances of the hemorrhoidal area are eliminated as causes.

Ulcerative Colitis

The salient features of chronic ulcerative colitis are a continuous or intermittent intractable, bloody diarrhea, and sometimes abdominal pain, anemia, fever and general debility. The inflammation of the colon is evidenced by a hyperemic and edematous, granular, easily bleeding mucous membrane or profuse exudate covering the lining, and, later, superficial and deep ulceration. The ulcers for the most part are confluent and shaggy, with indefinite borders and with

no special point of origin in the mucosa. The infection begins in the rectum and lower colon, and progresses upward to the cecum, sometimes invading the lower ileum. It may remain localized in the rectosigmoid region for months or years.

The mucosa first becomes red and congested with increased watery secretion and then it bleeds easily and finally breaks down into superficial ulcers (3). If the condition is severe, deep ulcers, going on to perforation, develop. Small, round-cell infiltration of the submucosa and muscular layers is very marked. One of the chief characteristics is the extreme thickening of the wall of the colon and the smoothing out of all the folds of the mucosa, leaving a smooth, glazed surface. This thickening is caused in two ways: early, by the hyperplasia in the mucosa and, later, by the fibrosis which develops in the deeper layers. After some time, the contraction of this fibrous tissue results in a marked narrowing of the lumen of the bowel, which is permanent and if localized may result in a partial bowel obstruction.

The disease begins practically always with dysentery, either starting gradually and becoming more severe, little attention often being given to it at first, or coming suddenly as a severe diarrhea. It may develop as an isolated case or as one of a number of cases in which the

patients are similarly affected by diarrhea, all of the other cases clearing in a short time, and this patient, though treated exactly like the others by the same physician, failing to get well. The diarrhea is at first watery; later, the stool usually contains some fresh blood and pus. The number of stools varies from two or three up to fifteen daily, which may keep up for several years, or the ulcers may become latent, similar to duodenal ulcers, and during this latent period, the bowels may become regular or constipated. As the rectum is most severely involved, tenesmus is often present; about one-third of all cases show this condition. Pain is not a severe sympton. In fact, it is more often absent than present, and when present it is seldom acute, unless due to a perforation. But there is more of a burning, uncomfortable feeling along the line of the colon. Abdominal gas and the expelling of excessive amounts of it causes complaint in one-third of the cases. As the ulceration is chiefly in the colon, digestion and food absorption are little interfered with until late in the disease, unless type of disease is severe; consequently, weight loss usually does not occur early. Loss of appetite as a result of the absorption of toxic products is also a factor in the loss of weight. Fever is practicall y absent until late in the disease, unless subacute peritonitis or perforation occurs. Blood in the stool will depend upon the

character of mucosal involvement. Some granular conditions without ulceration bleed freely, while some ulcers show no macroscopic blood.

Many patients are able to keep at work for years without much loss of strength or inconvenience, except for the frequent bowel passages, but the majority, after a greater or less time, if the diarrhea is constant, lose strength and are unable to keep up their work, although the hemoglobin and weight loss may not be excessive. This is no doubt owing to the fatty degeneration of the body organs, the liver especially, which takes place after the disease has existed for some time. In the remittent type normal strength may return during the periods of remission in the early years of trouble but, as time goes on, the weakness becomes more apparent. The disease is essentially one of many months and may be of many years duration, but when the breaking comes it is usually very sudden.

Perforation is not uncommon, and in itself is not always fatal without operation. The perforation, which comes slowly, is usually walled off into a localized peritonitis, with some pain and with slight fever and reaction. The body seems to be self vaccinated against the infection. Gastric complaint is rare, though occassionally late in the disease reflex vomiting may take place and be difficult to control. The patient is usually in good spirits

and inclined to look on the bright side of things until very late in the disease.

The beginning of the disease is chiefly in the early and strong periods of life, most of the cases starting between the ages of ten and thirty years. This is of course the period when most dietary indiscretions are indulged in and when most opportunity would be given through such indiscretions for a new organism to find lodgement in the bowel, or for the ever-present ordinary bacteria to take on pathogenic significance.

From the fact that the early stages of the disease are so often free from general symptoms, the simple home rem edies are used for a long time before medical attention is sought. When the usual medicines cease to check the trouble, it is let alone to continue as an inconvenience to the patient. Later when general symptoms begin to show themselves, medical aid is again sought.

The X-ray was not used indiagnosis of these cases until 1914, but since beginning its use, more of the extent of involvement has been shown (4), considering the relationship of the pathology in the colon to the X-ray findings, we would expect in the early stages of any dysentery to find an irritated condition, in which peristaltic action is rapid. Later on, hyperplasia of the mucosa develops and fibrous tissue is formed in the outer layers. This resultant

thickening causes interference with normal peristaltic waves. Each wave is lengthened and is not so deep, it has rounded not sharp, edges, and when the thickening in the wall of the bowel becomes marked, the colon becomes a stiff-walled tube without haustrations. Finally, with the contraction of the fibrous tissue, narrowing occurs and often stricture of the lumen results. This is shown in the radiogram of a typical advanced case by a small contracted colon, smooth without haustration. In an earlier case, the condition is present low down in the colon and just above the rounded, wide haustration or the sharply defined haustration, close together, showing either slight involvement or the spasticity of irritation (5).

Ulcerative colitis was first mentioned by Wilks & Moxon (6) in 1875, but was first described by White (7) in 1888.

Logan (8) believes that the underlying cause of the colitis is a metabolic disturbance.

Gross (9) was able to produce minute ulcers of the colon in 3% of a large number of rats on a diet deficient in vitamins.

Bassler (10) and others believe that Bacillus coli-communis is an important etiologic factor, asserting that this organism becomes especially virulent under proper conditions. Bassler ventures the designation of pseudodysentericus

coli for the organism found predominant in some of his patients. He also says that when the organism is injected intra-peritoneally into cats, rabbits, or guinea pigs, death occurs early.

Jex -Blake (11) considers as factors bacillus coli, proteus and pyocyaneus, and streptococci.

In 1907, Morgan (12) produced diarrhea in rats and rabbits by feeding a gram-negative bacillus, isolated from the stools of infants with summer diarrhea, differing from the ordinary dysentery bacillus in its sugar fermentation reactions. Einhorn (13), Hurst (14), and others seem convinced of this theory.

By the use of dextrose brain broth, B argen (15) isolated a gram-positive diplococcus and on lactose endo-agar, a gram-negative bacillus. Pure c ultures of each were injected into his experiemntal animals, the rabbit and also mixed cultures. Of 190 injected, 56 developed lesions of the bowel, only the lower half of the colon in many instances. Eleven of these had pure diplococcus and the rest, mixed cultures so he establishes this gram-positive diplococcus as the primary factor, its action being increased by presence of this colon bacillus. This diplococcus he isolated was plump, non-capsulated and with little tendency to grow in chains. On blood agar, it grew as an alpha hemolytic streptococcus.

The anerobes have been blamed as to etiologic significance in ulcerative colitis (16), in Filsen's report of satisfactory clinical responses by intestinal oxygenation but does not prove the importance of this bacterium in the etiology of this condition, for he himself suggests that the effect of such therapy may be on intestinal tissue proper.

There are some observers who present the idea that, for some unexplainable reason, the local tissue resistance of the colon becomes lowered, and organisms that are habitual saprophytes take on an added virulence and become pathogenic. This has been well expressed by Dr. T. R. Brown (17), Chief of the Gastro-Intestinal Clinic at Johns Hopkins Hospital, in the following manner:

> "Is it not possible that the cause of the disease is to be found not in the presence of a definite and specific infective agent, but rather in the absence of some protective substance or mechanism, or of something which normally inhibits the bacterial invasion of the intestinal wall, perhaps due to metabolic error, or endocrine disturbance or lack of a specific bacteriophage, or absence of some normal bacteriocidal substance in the intestinal mucosa?"

The view that chronic ulcerative colitis is an

aberrant form of bacillary dysentery persists in England (18), in Canada (19), and, possibly to a lesser extent, in this country. Ulcerative colitis appears to differ from bacillary dysentery in four particulars.

1. Ulcerative colitis is not known to present the abrupt, brief attack of the ordinary case of bacillary dysentery.

2. The age incidences are dissimilar.

3. Ulcerative colitis is not infective.

4. In ulcerative colitis bacillus dysenteriae is not encountered.

The first two difficulties are explained principally by Hurst and his co-workers by the hypothesis that ulcerative colitis is a modified form of bacillary dysentery. Actually, this may or may not be so, or the contention may be true only of a group of cases which may have begun as bacillary dysentery but which, when investigated, are diagnosed as idiopathic ulcerative colitis because of negative bacteriologic, parisitologic and serologic observations. As to the third objection, while ulcerative colitis is noninfective in that almost never are two cases found in the same household according to the records of the Johns Hopkins Hospital. Recurring or chronic bacillary dysentery with which it is comparable is regarded in many quarters as being noninfective too, especially when the offending organism, rarely isolated in this condition,

is not to be encountered. Fourthly, the bacteriology and serology of ulcerative colitis and that of recurring bacillary dysentery are not as dissimilar as would appear at first glance. In ulcerative colitis, bacillus dysenteriae is not to be found. In chronic bacillary dysentery, these organisms are rarely to be encountered. Their scarcity, when discovered, and the severity of the disease are such that the causal relationship of these bacteria to the lesion of chronic dysentery is somewhat incredible. In ulcerative colitis, the serum agglutination reactions with bacillus dysenteriae are negative. In a majority of definitely established sub-acute and chronic bacillary dysenteries, Douglas, Colebrook,, and Morgan (20), have shown that the serum agglutionation reactions are of no diagnostic import. There has been shown in dysentery a relationship between the diminution of agglutination properties and the increase of time elapsing between the onset of the attack and the performing of the agglutination test. Incidentally, it has been noted that many cases finally diagnosed as chronic ulcerative colitis are studied intensively for the first time years after the initial attack. Thus, it is possible that the differences between chronic ulcerative colitis and chronic bacillary dysentery may be quantitative and not qualitative, at least in some cases.

In 1933, Paulson (21), learned that in undiluted

and in dilutions of n oncoagulable human blood (1 cc of blood to 3 cc of saline solution) in normal and bacillary dysentery cases, bacillus dysenteriae Shiga and Flexner failed to survive on incubation at 37degrees C.; in bouillon controls they grew abundantly. The experiments suggested that the continued presence of fresh blood in the intestine might in a measure explain the inability to isolate these organisms from many with chronic bacillary dysentery and in some other patients, who in consequence of this as well as of negative, parasitologic and agglutination studies are classified as having chronic ulcerative colitis.

Ulcerative colitis and recurring or chronic bacillary dysentery are thought by many to be identical in these respects: The clinical course of the two conditions is hardly distinguishable. Pathologically, the appearances of the large intestine in bacillary dysentery and ulcerative colitis are not to be differentiated. Chronic bacillary dysentery, like chronic ulcerative colitis, usually involves the distal portions of the large bowel; in exceptional instances in both conditions, the lesions appear to be restricted to the more proximal segments. In acute bacillary dysentery, as in ulcerative colitis, the process attacks the mucosa with early rectal involvement (22). Even many of the complications observed as occurring in ulcerative colitis, such as fibrosis, strictures, polypi, perforation, joint

changes, and transient paralyses sometimes involving muscular atrophy, are noted by MacCallum (23), as complications of bacillary dysentery. Buie (24), who wrote that the rectum and lower sigmoid were characteristic in chronic ulcerative colitis, states, in speaking of the pathology of this condition, "I am willing to concede that this picture is variable enough to keep me somewhat in doubt as to its various manifestations."

From the foregoing data, it appears that ulcerative colitis meets the requirements of a syndrome rather than of an entity. It is a set of symptoms and the sum of signs of a morbid state, the etiology of which is either unknown or, like bronchial asthma, variable. Its clinical course, with its pathologic manifestations, complications and sequelae, are indistinguishable from chronic bacillary dysentery, thus rendering its characteristics not specific for idiopathic ulcerative colitis.

Facal infection has been thought to be of etiologic importance by Cook (25), and others. Obviously, eradication of all sources of infection should be undertaken. Relief thought to be so obtained often may be purely coincidental because of the self limited tendency of the acute phases or possible of some influence of other associated forms of therapy.

According to Paulson (26), in a discussion of

Bargen's (27), work on the diplococcus, a diplococcus may be a pneumococcus, an enterococcus or one of many varieties of streptococci. When observed as young cultures in liquid mediums, when smeared from solid mediums or from material secured directly from the bowel, these organisms - even those streptococci which in older liquid cultures or in subcultures may present characteristic chains - appear as diplococci. Occasionally, diplobacilli, diphtheroids, staphylococci and small, plump gram-positive bacilli on direct smear, as well as from early cultures in liquid mediums, especially when the cultures are mixed, may be indistinguishable from diplococci. Obviously then, a diplococcus is not distinctive; morphology is not characteristic, it is merely descriptive.

In 1925, the diplococcus was reported by Bargen (28), as that of an alpha zoned bacterium, which never ferments inulin or mannite. In 1927, Bargen (29) added that of 105 strains tested, 41 fermented mannite and 64 did not. In 1930, Bargen (30) reported that the diplococcus does not usually ferment mannite, but lacks the power to ferment inulin.

From the foregoing account, it is evident that the etiology of ulcerative colitis is not solved. Perhaps, it can best be summed up by quoting Smith (31), who said, "It is clear that no pathogenic agent has been identified as

the cause of this disease. It is possible that allergy, through a modification of the Schwartzman phenomenon, might be the explanation. It seems more plausible, at the present time, that neurogenic or toxic spasm of the colon musculature can produce an ulcerative, hemorrhagic inflammation of the mucosa, and that various secondary agents might exaggerate or perpetuate such a reaction, producing the typical pathological picture of necrosis and proliferation."

Not knowing any specific cause for these internal ulcers, Logan (32) applied the principles, insofar as possible, of treatment that would be applied to an ulcer on the external surface of the body. Soothing and "healing" drugs were alternated with those which stimulate chronic, indolent ulcers. Olive oil was early found to be a good tissue-builder and soother, and is the one agent that stands out as having given the best results. It is taken by mouth, three to six ounces daily, with from 60 to 90 grains of bismuth. An enema of 3 ounces of olive oil and 60 grains of bismuth is given every night with the patient in knee-chest position, in order that it may be retained as long as possible. Various other sedatives and antiseptics have been tried but are not as good as the olive oil and bismuth.

The greatest benefit in the treatment of patients has come from the use of heat. With the idea of producing

a kind of Bier's congestion, enemas of hot water (120 degrees F., when it enters the rectum) were given, and in two cases, in which the involvement was in the rectum and in the rectosigmoid only, healing resulted with the disappearance of all symptoms after four months of steady treatment. The enemas are given twice daily for from twenty to thirty minutes. Care must be taken not to distend the bowel, a double rectal tube being used. For those cases, in which the entire colon is involved, enema treatment is of use only in checking tenesmus and rectal irritation, and for the healing in the lower bowel.

Surgery was undertaken first with the idea of introducing medicine through the upper end of the colon and irrigating through; thus, appendicostomies were first done (33). Later, with the idea of removing infected and irritating material and preventing it from passing over the ulcer, thus giving rest to it, cecostomies and ileostomies were done, and afterward the distal ileum was brought into the wound (34).

Derivatives of sulfanilamide have been used in the treatment of chronic idiopathic ulcerative colitis for several years (35). From the Mayo Clinic encouraging results have been reported (36) with the use of neoprontosil. Other writers, however, have found this drug to be of little value. It has been the feeling of some observers

that certain sulfonamide derivatives are efficacious in the treatment of ulcerative colitis, but that toxic manifestations often make it necessary to discontinue therapy before the best results can be attained or properly evaluated.

Recently, sulfaguanidine, a water soluble sulfonamide derivative which is poorly absorbed from the gastro-intestinal tract and has a high anti-bacterial activity, has been described in its action by Bornstein and Strauss (37) because these properties had suggested the possible effectiveness of sulfaguanidine in the therapy of infections localized in the intestines, since high concentrations can be attained in the gastro-intestinal tract, while the blood and tissue concentrations remain low. They studied the action of this drug on different Salmonella groups and noted a marked bacteriostatic effect on escherichia coli, eberthella typhi, and Shigella, but concluded that its use for types other than the susceptible ones was perhaps contraindicated since the pathogens may flourish while the non-pathogenic organisms are suppressed. In my perusal of the literature there was much variation in analyses of results, but considerable uniformity in statistics. Before treatment, the organisms usually found were hemolytic E. coli, hemolytic streptococci and non-hemolytic E.coli, Bargen's bacillus and an anaerobic mixture. After treatment, the hemolytic organisms were greatly reduced or absent in every case. The drug had little

effect upon the colon bacillus. No correlation could be observed between the disappearance of the hemolytic organisms from the stool and the clinical condition of the patient, nor was there any relationship between the apparent effectiveness of the drug and the duration of the disease.

The recent literature on chronic ulcerative colitis continues to demonstrate the contraversial status of all phases of this problem.

One thing stands out in the management of this problem; that until it is possible to point to the causative factor or factors, the preliminary study must include a careful diagnosis and evaluation of all the factors that may enter into the picture of this disease. Until the specific organism of ulcerative colitis is isolated or the exact vitamin deficiency which is responsible is demonstrated or the allergic factor definitely established, it is best for the clinician to realize that he is thus far not treating a bacterium, an amoeba or a virus, not solely replacing vitamins, not alone playing the role of an allergist, but that instead he is treating a complex human being with all the considerations, emotional and otherwise, that this implies.

In the acute stage of this disease, complete bed rest is of course essential. If there has been a substantial blood loss from the bowel, replacement therapy by frequent transfusions is helpful. Even in the absence of marked

anemia, transfusions are helpful. Abdominal pain is at times severe enough to necessitate sedation. Powdered opium or codeine usually suffices to give symptomatic relief but of course must be used judiciously because of chronicity associated with the disease. Dehydration may be marked and fluids should be given in the form of normal saline, as the blood chlorides are frequently reduced. Plasma is useful in this stage if hypoproteinemia and edema are present. It is difficult during this acute phase to keep the nutritional requirements adequately supplied, but every effort should be made to give sufficient food by mouth, at least to tide the patient over this acute period.

Most authorities have become cautious in advocating the use of such drugs as sulfanilamide and neoprontosil in the desperately ill individual. The use of sera or vaccines at this period of the disease depends in a large measure upon the physician's belief in the efficacy of sera and vaccines for this disease in general. In the acute stage, perforation of the colon may occur and this is a definite indication for immediate surgery.

The chronic phase of the disease is the most perplexing and most taxing problem that the physician may have to meet. The gastric acidity should be determined. Many patients with ulcerative colitis have a low gastric

acidity or a complete achlorhydria. Dilute hydrochloric acid in these cases will reduce the flatulence. Rest is essential, but some common sense must be used as the patient's whole mental attitude may be so affected as to bring about a deleterious reac tion, especially as regards absolute bed rest. Certain moderate exercise, not bringing about any physical or emotional strain, seems to be the procedure of choice insofar as general physical status is concerned.

The diet is a difficult problem. Anorexia is almost always present, and to maintain adequate nutritional requirements will be another "headache" to the physician and dietician. Often patients may attribute their diarrhea to some one or many foods. When the patient is having eighteen or twenty stools a day, some of them are bound to come immediately after feedings. It is the physician's lot to convince the patient that the fanciful and deficient diet that he is imposing upon himself is unnecessary and harmful. Most authors agree that a diet high in calories, vitamins and protein and low in residue is best. It is not important or advisable to eliminate vegetables, but they should be pureed. By frequent small feedings the total caloric intake may be maintained.

Mackie (38) found that 62.6 percent of his 75 reported cases of ulcerative colitis showed evidences of vitamin deficiency. Whether this deficiency preceeds the

changes in the bowel or whether it is produced by the diarrhea, dehydration and limited food intake, is not entirely clear. However, it is probably that these deficiency states are secondary to the bowel changes. It is agreed by all, however, that vitamin replacement is important. Vitamin D should be given. The marked hemorrhagic tendency which appears in the disease suggests the possible relation to a deficiency of vitamins C and K. Bargen and Vickers (39) reported benefit from vitamin C in severe hemorrhagic cases. It may be administered orally in large doses. In searching for clinical results from administering vitamin K, there is a recognized shortage, but it is thought to be due to the intestinal dysfunction and liver damage rather than the cause but certainly may be of importance in secondary manifestations of the disease (40).

Administration of the entire vitamin B complex is worth while. Yeast is not a satisfactory source of these vitamins, as it increases the abdominal distention. There is no evidence that liver therapy in ulcerative colitis has any specific or uniformly beneficial results. However, it does supply some vitamin B and may be of value to stimulate bone marrow function for replacement of blood cells lost in hemorrhage. The use of crude liver extract rather than the more concentrated should be more effective if vitamin replacement is the important factor.

If there is evidence that absorption from the small bowel is poor, vitamins should be given parentally or intravenously.

Of course, sulfanilamide was sooner or later to be tried in ulcerative colitis. The writers conclude that some benefit results in the early stages of the disease or where the process is relatively mild. They advocate giving from four to five Gm., divided into five equal doses daily and continuing this dosage from ten to fourteen days. The dangers of sulfanilamide in this disease have become more apparent with its widespread use. Severe toxic reactions have been numerous. Jaundice has been reported in many cases following the use of sulfanilamide. A toxic rash and a sharp increase in the pyrexia as well as an increase in the number of stools have also been noted. The consensus of opinion now is that sulfanilamide should not be used except in rare cases. When it is employed, the blood level of sulfanilamide should be determined at frequent intervals. The drug should be discontinued at the first sign of hepatitis. Because of the toxicity of sulfanilamide in these cases, neoprontosil has been substituted. It is a comparatively innocuous drug and there have been no reports of liver damage. Bargen (41) reports very favorable response in his series of cases. However, the majority of other reports have not been so glowing. In fairness to Bargen,

however, it should be stressed that he did not claim that this was a specific agent, but that it was a safe and helpful adjunct to vaccine or serum.

Sulfaguanidine has been available, even for experimental use, for only a short period, and no accurate conclusions can be drawn as to its true value, since exacerbations and remissions are the usual course in this disease. There have been no undesirable effects from the use of sulfaguanidine in massive doses, except for an occasional skin rash.

The use of sera and vaccines of various kinds has steadily lost favor in the past ten years. There has been much discussion of a specific diplostreptococcus, known as Bargen's bacillus, as the primary etiological factor. This concept has not received universal acceptance, and the weight of opinion probably rests with the statement that this diplococcus, if it is a single organism at all, is one of the predominating secondary invaders. Since Bargen's original article (42), almost no competent observer has been able to isolate an organism which conformed consistently to the morphological, cultural and heat requirements that Bargen set forth. Mackie (43) states that strains of the diplococcus received from the Mayo Clinic have been found to differ among themselves in their behavior as to culture and heat resistance. More recently anaerobic bacteria,

such as actinomyces necrophorus, have been advanced as primary agents. Most of the bacteria recoverable from the human colon have at one time or another been suggested as important etiological factors. Autogenous rather than stock vaccines should be used if vaccines are employed at all. The great number of anti-bacterial measures advocated suggests the inadequacy of all. Protein shock seems helpful in some cases, and suggests that this is the explanation for the results Hurst (44) obtained with anti-dysentery sera.

Colloidal aluminum hydroxide, kaolin, olive oil and azochloramide by rectal instillation have all had their day. They appear to be not only useless but at times harmful. It probably is wise to stay out of the colon except for an occasional proctoscopic examination to determine the progress of the disease.

There is great difference of opinion as to the role that surgery should play in cases of ulcerative colitis. The position taken by most writers in regard to surgery depends in a large measure upon their opinion as to the efficacy of medical measures. As an illustration, in the Mayo Clinic since the advent of "specific therapy", the number of cases treated surgically has declined from 26 percent in the period from 1919 to 1923 to 1.4 percent from 1929 to 1936 (45). On the other hand, those who have had less favorable experience with medical management employ

ileostomy and analgous processes in as many as 65 percent of the patients with this disease (46).

The indication for surgery may be either obligatory or optional. Included among the absolute indications are perforation of the colon, a fulminant type of the disease, and complications, such as crippling generalized arthritis, repeated hemorrhage from the colon, and severe perirectal infections. Among the optional indications for surgery are failure to achieve clinical improvement, persistence or progression of the lesions as seen by proctoscopy, X-ray evidence of progressive fibrosis of the colon with pseudopolypoid degeneration of the mucosa, and progression of the complications attributable to chronic sepsis. The exact surgical procedure in these cases is not the subject of this paper. However, the operations frequently performed in the past, such as appendicostomy, cecostomy, and double bowel colostomy are based on a false premise - namely, that medicated irrigation will eliminate the infection and that these procedures will produce physiologic rest of the colon.

An ileostomy appears to be the surgical procedure of choice, as it completely diverts the fecal stream. At a subsequent time, removal of the entire colon, preferably in three stages, may have to be carried out. Before surgery is entered upon, the patient should be thoroughly acquainted with the fact that in all probability he will

have an ileostomy the rest of his days. It is only fair to acquaint him with the inconveniences of this fecal short-circuiting.

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