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**The Medical Management of Chronic Ulcerative Colitis**

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THE term "chronic ulcerative colitis" refers to an infectious disease of which clinical, pathologic, and bacteriologic features are characteristic. The condition is poorly named, for such a nondescript term could include many kinds of ulcerative disease. Perhaps the term "colitis gravis", which has recently come into use, would be more descriptive.

The condition is a destructive infectious disease of the colon, of which intractable bloody dysentery is the most striking feature. It may begin insidiously or in a fulminating way and great bodily depletion will occur quickly. The disease is comparable, in its damaging nature and progression, to advancing tuberculosis.

ÆTIOLOGY

In considering so serious a disease of the large intestine it is perhaps well to mention contemporary ideas of ætiology before describing in detail my own views about this important part of the subject.

Foremost among these ideas is that held by a few investigators, that chronic ulcerative colitis is the end-stage of an infection by micro-organisms of what used to be called the colon-dysentery group, and which now would include colon bacilli, dysentery bacilli, and paradysentery bacilli. Their belief is based on the finding of these micro-organisms in a few cases of ulcerative colonic disease, a slightly elevated concentration of antibodies of these organisms in the blood of a few patients, and the therapeutic response of some of the patients to administration of antidysenteric serum. Since no evidence that these organisms are ætiologic of the condition has been encountered in our cases at the Mayo Clinic, even when intensively studied serologically and by all accepted methods for isolation of these bacteria, I have been loath to accept this concept of causation of the disease.

Another belief concerning ætiology has as its basis the idea of infection by a

variety of organisms. The thought has been that many kinds of bacteria, under special conditions, may initiate the pathologic process, and may be responsible, in some instances, for its continuance. By virtue of this line of reasoning, colon bacilli, pneumococci, staphylococci, and other bacteria have been credited with initiating this serious pathologic process. Recently Schwartzmann and Winklestein have brought forward some interesting data suggesting that secondary invaders may play their part in advanced cases of this infection. It has been thought by some that the normal intestinal inhabitants assumed virulence, in association with failure of the body's defence against them, as in cases of mucosal injury and in the presence of dietary or other deficiency.

This, then, suggests a third theory of ætiology, namely the one concerned with deficiency of vitamins, minerals, or other substances. Lesions of the skin, œdema associated with disturbance in plasma proteins, peripheral neuritis, abnormalities of the inorganic constituents of the blood—and other evidences of failure of proper absorption of certain essential foods—have been noted in cases in which patients have been seriously ill with advanced and destructive chronic ulcerative colitis. However, it must be remembered that in a disease in which such terrific hyperperistalsis occurs, such evidence of states of deficiency must be regarded as rare complications rather than as integral parts of the morbid mechanism of chronic ulcerative colitis. The very fact that they occur only in the advanced and extremely destructive stage of this disease of the intestinal wall, makes it clear that they are late complications. Those investigators who have felt that the symptoms of deficiency were of primary importance, and attributable to improper intake of food or to failure of absorption before inception of the state of disease, very likely are hitching the cart before the horse. Repeatedly I have assigned to physicians associated with me the task of inquiring into the life-habits of patients who had chronic ulcerative colitis. Such studies have been carried out on many series of patients who have presented themselves for treatment of chronic ulcerative colitis. All investigations of this type have been unproductive of any evidence of vitamin or other deficiency playing any part in the causation of this disease.

A fourth hypothesis relative to the origin of this disease has to do with a disturbance of body metabolism, such as occurs in diabetes, goitre, and similar diseases. The thought behind this may have some rationale but, so far, experimental evidence is not at hand to substantiate it. Increased activity of duodenal enzymes was found by Brown in some of these cases.

A fifth hypothesis has been suggested, namely that residual infection following infestation by amœba and other parasites, is the cause of ulcerative colitis. Clinical and experimental evidence has refuted this idea.

Available evidence points to the view that this disease is caused by infection by a specific micro-organism, or by a group of micro-organisms. From the standpoint of infection it is somewhat similar to pneumonia. In pneumonia there is a violent pulmonary infection by the pneumococcus and some types of streptococcus. Nevertheless, the pneumococcus is usually thought of as the cause of pneumonia, because it is found in the lesions in so large a percentage of the cases. Chronic ulcerative colitis is a severe, destructive, colonic infection, associated in many cases with fever and all the symptoms of intense toxæmia. In the less severe cases, it can be thought of, as far as its characteristics as an infection are concerned, as comparable to severe bronchitis merging into bronchopneumonia. Extensive experimental and clinical investigations by many workers have established a diplostreptococcus of characteristic morphologic and biologic properties as at least one of the main instigators of this disease.

Establishment of this fact grew from the idea that the causative organism might be sensitive to oxygen, and that perhaps a medium affording a gradient of oxygen tension would serve to enhance the growth of the causative organism, to the

exclusion of retardation of growth of other common intestinal inhabitants. A conveniently prepared medium which furnishes these requirements is Rosenow's dextrose-brain broth.

Our experience has taught us that the best and quickest way of isolating this diplostreptococcus is by obtaining material for culture through the proctoscope, directly from the bases of rectal lesions. Also, in many instances, careful study of the purulent, bloody, rectal discharges of patients who have chronic ulcerative colitis has revealed that the predominant organisms are diplostreptococcal forms. Very frequently these organisms can be cultured directly from the discharges. In smears of the rectal discharges the streptococcal forms are so common that other forms of bacteria are often not seen. The organism so isolated is not the enterococcus described by Houston and McCloy, and there are many characteristics that distinguish it from the common enterococcus. It has been isolated from approximately 80% of the patients with chronic ulcerative colitis whom we have examined. Its injection into animals has produced lesions essentially like those found in man. Occasionally too, the organism has been obtained and cultured from the blood of patients whose condition was in the severe, fulmination stage. It may also be significant that tonsillectomy, removal of infected teeth, and acute infection of the upper part of the respiratory tract, have caused marked acute, although temporary, exacerbations of the disease. The diplostreptococcus has been found about the teeth, in the tonsils, and in other portions of the upper part of the respiratory tract. Following out this thought, the pulp of the canine teeth of dogs was removed and the pulp cavities were packed with dense suspensions of these diplococci. Peri-apical abscesses developed and between eight and twelve months later the dogs presented the typical clinical and proctoscopic picture of chronic ulcerative colitis. Occasionally, too, the streptococci have been isolated in pure culture from perirectal abscesses occurring in the course of the disease. Many other facts have been encountered which lead us to the belief that the inciting factor in this disease is a particular type of streptococcus.

Some definite and significant factors which predispose to invasion by this organism have come to be recognized. The most common of these are infections of the upper part of the respiratory tract, including tonsillitis, cranial sinusitis, bronchitis, and pneumonia. It is not uncommon for so-called severe colds to be followed by an intestinal upset, and this may eventuate in real ulcerative colitis. The much-used term "intestinal flu" may be a misnomer of the forerunner of this type of colitis. Extensive upper abdominal operations have occasionally been followed by fulminating attacks of chronic ulcerative colitis. Distant foci of infection in the tonsils, pulpless teeth, and the gall-bladder, have been known to initiate an attack of colitis. Anal infections at times have been the origin of this infection. Lack of free hydrochloric acid in the gastric content has seemed, in a few cases, to predispose to this malady. Previous intestinal disturbances, such as amoebic colitis and so-called mucous colitis, may have been followed by this disease in a few instances, but only in the sense that intestinal trauma may lay the groundwork for this infection. Occasionally people in normal health have been found to be carriers of this organism. A few cases of vague intestinal unrest have been seen in which the colon appeared normal, but the stool contained the typical streptococcus, and the patients returned later with definite ulcerative colitis.

No particular type of individual is more prone to this disease than another, and no particular race of people is particularly susceptible. The ages of patients afflicted with chronic ulcerative colitis are those of most patients who have chronic infections. Patients 2 years of age, and others 80 years of age, who apparently had acquired the disease recently, have been seen, but the majority of patients are in the second, third, or fourth, decade. The condition has been found in all parts of the United States, Canada, South America, and Europe. Most of our patients have come from

the north temperate zone, and the middle-western regions of the United States of America, a few patients have come from foreign nations, and one has come from a South Sea island. Rarely has the condition been found to afflict more than one member of a family. In one series of 1,600 patients studied, about eighteen instances of affliction of more than one member of a family were found. It may be said, however, that in these few instances the members so affected were usually those who "were rather close" in the family. In no case have husband and wife been affected. In one family recently observed four members were afflicted at different times in a period of ten years.

The only relation which climate seems to have to the disease is from the standpoint of infection of the upper part of the respiratory tract. A climate which predisposes people to frequent respiratory difficulties is prone to be a factor in initiating the disease, as well as in causing its recurrence. There is little reason to suspect diet to have much to do with the origin of this condition, for patients of all races, eating all kinds of food, sometimes in very limited, and sometimes in very large, amounts, have become afflicted with chronic ulcerative colitis.

In some cases the causative organism is, no doubt, already present, and does not give rise to symptoms unless resistance becomes low, because of the presence of a systemic disease, because of inherent susceptibility, or because of a factor which is local in its effect, such, e.g., as strenuous catharsis.

#### PATHOLOGY

It is fortunate that in this disease the sigmoidoscope makes possible observation of the pathologic changes in the living patient, from the inception of the disease to its well-advanced state. Much can be learned, moreover, through digital palpation of the intestinal wall. Study of the pathologic changes after death has also been thorough.

The earliest changes demonstrable by proctoscopic examination are those of a diffuse inflammatory reaction in the mucous membrane of the colon. These changes begin at the lower limit of the rectum and extend upward. In approximately 20% of cases the process will be found limited to this lower portion of the colon, and in this percentage the upper limit of the process will be seen to fade out gradually into normal bowel. There is no sharp line of demarcation between healthy and abnormal tissue. Closer study of the mucous membrane—gained by use of a magnifying attachment applied to the proctoscope, which increases the sizes of objects about eight times—reveals numerous small hæmorrhages scattered about in the diffusely inflamed mucosa.

Definite distinction between the first stage and the second is not always possible. However, separation into stages is warranted, because in the second stage an additional characteristic appears in the guise of œdema of the mucous membrane. This œdema is diffuse, and involves the same area as that of the hyperæmia seen in the first stage; the mucous membrane now appears thick, red, and boggy. It is so easily traumatized that only slight contact of the metallic end of the examining instrument with the diseased intestinal wall is sufficient to cause bleeding. The ecchymotic spots are now more apparent.

In this hyperæmic and œdematous mucosa, little spots appear immediately beneath the mucous membrane, resulting in the third stage of this pathologic development. They are yellowish, and there is little, if any, elevation of the mucous membrane over them. Such miliary abscesses are scattered diffusely throughout the wall of the diseased portion of the bowel. They are not follicular abscesses. There is no connexion between the arrangement of the abscesses and the situation of the follicles, and there is no lymphoid tissues associated with them.

The miliary abscesses ultimately overcome the limiting effect of the superficial lining of the mucous membrane, and rupture through it, leaving open ulcers. These

are the miliary ulcers of chronic ulcerative colitis, and now the wall presents the typical diffuse, granular, bleeding "moth-eaten" appearance, the fourth stage of chronic ulcerative colitis.

The four stages represent the active phase of chronic ulcerative colitis. However, they will be observed only in those cases in which the disease has not been present previously. The disease is characterized by periods of exacerbation and remission, and after one attack has subsided the wall of the bowel will present many variations in appearance. These variations are attributable to the fact that, once the disease has appeared and healing has taken place, the mucous membrane and other layers of the wall of the bowel are altered. There are deposits of fibrous tissue in the mucosa, and consequently, in a period of exacerbation characteristics are present which are not ordinarily seen in the first attack. Probably five separate stages, therefore, should be recognized, because there are four stages of activity and one stage which covers the period of remission.

In subsequent attacks, many varied and bizarre changes develop in the wall of the bowel. These are attributable to, and are modified by, the severity and number of previous attacks, and by the amount of deformity which has been produced in the walls of the bowel. The hyperæmia, œdema, miliary abscesses, and miliary ulcers, will be seen in regular order in those parts of the mucous membrane which are not deformed and scarred, but this progression of events will not be present in those areas in which the mucous membrane has been destroyed and replaced by scar tissue. In place of these characteristic features, in the fibrous areas will be found miliary, pock-like scars which are of equal significance with any of the features mentioned. In severe cases, in which no mucous membrane is left unattacked, these scars are of greatest importance, because they represent the chief gross evidence of chronic ulcerative colitis. They are the "footprints" of the original attack.

In addition to these miliary scars, the fibrous wall of the bowel will be involved with other, irregular, types of ulceration. The ulcers will vary in diameter from 2 or 3 mm. to 1 or 2 cm. The bases are superficial, and the margins adhere closely to them. This is the secondary, infective type of ulcer, and may possibly be attributable to infection of the original ulcer by other types of organisms than those which caused it, after the abscesses have ruptured. It is not surprising that confusion arises from this appearance of the bowel, when the only gross evidence that can be relied on for making a diagnosis in this stage is the presence of the pock-like footprints.

Contraction of the wall of the bowel is a constant feature, and is one of the cardinal diagnostic characteristics of chronic ulcerative colitis. As seen through the proctoscope, this "stricture" is uniform, and may vary from the slightest degree of contraction to a stricture through which it is impossible to pass an instrument of greater diameter than the average cystoscope. When the disease has progressed to this extent, it is possible to distinguish few of the characteristics of the disease as they have been described; only a bleeding, ulcerated tube is seen.

#### DIAGNOSIS

Much can be learned of the nature of any given case of dysentery by careful review of the patient's history. A presumptive diagnosis of chronic ulcerative colitis can frequently be made from the history alone. The history may be one of two types. In one type the patient relates that the onset was slow and insidious, beginning with only a slight increase in number of evacuations of the bowel, but soon blood and pus were passed with the stool. The movements may have increased rapidly in frequency, or at least the number of bloody, purulent discharges may have increased. In the other type the physician is told that the illness began in a fulminating manner, associated with fever, malaise, copious, bloody, purulent diarrhœa, anæmia, and rapid depletion. Loss of weight may be very alarming and

attributable to many factors—among them, dehydration, frequent evacuations of the bowel, extreme toxæmia, and loss of appetite.

A patient may have the milder form of the disease for months or even years, and then it will suddenly change into the fulminating form, or the change to the fulminating form may be by slow progression. By the time the change has taken place the pathologico-anatomic features will be identical with those of the fulminating form. I emphasize this fact because a suggestion has been made by some physicians that the two forms represent two different diseases and that treatment of the two should be quite different. We have considered the two forms rather as different degrees of severity of the same disease. In the fulminating form the infection is more violent and more massive than in the milder form and the patient's resistance is minimal. In the milder form, resistance to the infection is greater, and constant effort is being put forth by the host to dissipate the disease. In the advanced case, existence of chronic ulcerative colitis can often be suspected from the patient's general appearance. The face is drawn and anxious, and there is a strange, greyish-yellow pallor. In earlier cases these signs may not be exhibited in any striking way. Pain is not a prominent feature of this disease but straining at stool, with frequent griping and tenesmus, is very common. These difficulties probably have a mechanical basis, at least in part, for the bowel in this disease narrows to a funnel as it approaches the rectum. In the more severe cases, and particularly if patients are bedridden, a morbid bodily odour may prevail. In general, results of treatment vary directly with the mildness of the process. The more intestinal destruction that has occurred, the more prolonged the treatment will have to be and the less will be the possibility of complete relief of symptoms.

#### TREATMENT

The attitude toward the disease in the last decade has changed from one of hopelessness, as far as medical care is concerned, to the belief that the condition constitutes primarily a medical problem. The attitude of despair has been replaced by one of hopeful accomplishment. It is well to think of this disease as the modern practitioner thinks of tuberculosis. One should speak, not of its cure, but of its control.

Treatment should rest on the following convictions: (1) That the condition is an infectious disease of the large intestine, (2) that uncomplicated cases constitute medical problems, and (3) that certain complications are definite indications for surgical operation.

The following complications are in the field of the surgeon: neoplasm, polyposis, stricture, perirectal abscess, perforation, and massive rectal hæmorrhage. Most of the other complications, however, such as arthritis, cutaneous lesions, renal insufficiency, endocarditis, phlebitis, nutritional œdema, arterial occlusion, peripheral neuritis, and other conditions associated with great depletion, fall in the realm of the internist. In 85% of cases there are no complications.

Our treatment readily divides itself into: (1) Rest and restful recreation. (2) Diet. (3) Serum and vaccine. (4) Nursing care. (5) Drugs. (6) Transfusions. (7) Supportive measures. (8) Irrigations and instillations. (9) Removal of foci of infection.

(1) In the acute fulminating case, rest in bed and absolute quiet should be maintained until the patient is free from fever, and then there should be a very gradual return to physical activity. To rest the intestinal tract it may be necessary to withhold food by mouth and to give fluids parenterally. For the more chronic, although severe, case without fever, restful recreation is important. By this is meant that the patient should not be kept in bed but should have a very positive programme of mild activity. Reading, short walks, and mental diversion are helpful. These patients easily become discouraged. The slightest change in symptoms which is not for the better may undo days of improvement because of a patient's mental attitude toward such a change. Patience and perseverance on the part of the

physician, and an optimistic viewpoint, are essential. Occupational therapy in many forms can be made very interesting. This type of diversion is invaluable, for it tends to distract the attention of the individual from his need of remaining near a toilet room.

(2) The feeding of the patients presents one of the most difficult dietary problems in medicine. It seems that in the past many physicians have restricted too greatly the amounts of food allowed to these patients, and as a result the patients have lost in strength and in their ability to fight the infection. In the active stage of the disease there is invariably a lagging of appetite, or complete anorexia. The problem, then, is first that of creating an appetite, and next, that of giving foods which are digested almost entirely in the stomach and small intestine, and which thus leave very little residue for the colon. The foods prescribed should vary with the stage, severity, and complications of the disease. When the symptoms are acute, the patient may be able to take only a small amount of highly concentrated food. In the more severe cases, it may be necessary for a time to give nothing but liquids by mouth. In the worst cases a solution of glucose can be injected intravenously and large amounts of physiologic solution of sodium chloride can be injected under the skin.

For the average case, however, the essential features to be considered in the diet are that it shall not be irritating, that it shall be of low residue, that it shall be high in proteins, that it shall have an adequate content of calories, vitamins, and minerals, and that it shall be offered as attractively as possible. Proteins in most forms are very desirable, vitamins can be supplied in concentrated form in fruit juices, yeast, butter, wheat germ, cod-liver oil concentrate, or irradiated ergosterol. Contrary to the usual assumption, milk is not a low-residue food, and is not well tolerated by many patients. Boiling the milk makes it slightly more digestible. It is very often necessary to begin the treatment of these patients in the hospital, where their activities can be accurately controlled, even though they may not be acutely ill. On this basis a very definite dietary programme can be outlined. On admission, the patient is given strictly bland food, to which additions can be made at regular intervals.

Although the diet is thus based on broad, general principles, it must still be made individual, for, as with many other conditions, few patients react similarly to any given programme. It must be graded up or down to fit individual needs.

(3) The specific antibody solution (concentrated serum) administered to these patients has been prepared by immunizing horses against many strains of the diplo-streptococcus found in the diseased tissues. It has been administered in the acute, fulminating cases, and in the chronic cases, until improvement has occurred. The concentrated serum is administered deeply into the muscles after the patient has been desensitized by small, intracutaneous injections. In the more resistant cases, better results are obtained by intravenous administration of the serum. Injections are given about every twelve hours, beginning with 0.1 c.c. of the concentrated antibody solution, increasing each injection by 0.1 c.c. until the average maximal amount of 3 c.c. has been given. This is graded up or down according to the patient's tolerance. Improvement in the patient's symptoms usually runs parallel with the local or systemic reaction to the serum. A local reaction of the type usually seen with administration of any serum is the rule; generalized serum sickness occurs but rarely.

When improvement comes, and in milder and earlier cases, a bacterin, prepared as an autogenous vaccine from the organism found in the rectal ulcers, in each case, is administered subcutaneously. This is given at intervals of from three to five days for several months, beginning again with a dose of 0.1 c.c., increasing each injection by 0.1 c.c., up to the average maximum of 1.5 c.c. After a rest of several months, the same procedure is repeated. Three or four such courses are

administered, or the vaccine is given until the patient is free from symptoms. After that an occasional course of vaccine is given for several years.

Antidysenteric serum of the type used in bacillary dysentery has given favourable results in a few cases, but in many cases the serum sickness has been so severe that the good effects were nullified. It is to be hoped that the new colon bacillus serum advocated by Swartzmann and Winklestein may prove of additional help in some of the fulminating, resistant cases.

(4) It has been intimated that many of the patients who have this type of colitis are so ill that hospital treatment is advisable. Rest in bed is usually prescribed for the initial part of the treatment, and often for weeks during an acute exacerbation. The systematic execution of the many details necessary for comfort and peace of mind, as well as for actual physical progress, can be accomplished only by careful nursing, which may be by the hospital staff or by helpful individuals in the home. Freedom from worry and emotional strain is important. Fatigue and nervous excitability interfere with a patient's progress. It is important to keep the patient warm and to maintain the body fluids. Occasionally hot abdominal stupes seem to give much comfort. The great urgency to movement of the bowels which seizes these patients, and to straining at the stool—to which they are so prone—must be allayed. This can be done by judicious psychotherapy. Sufficient sleep is most helpful. The many little comforts which are accorded patients who have any serious illness cannot be over-emphasized in these cases.

(5) No single drug has been found that will help more than an occasional patient. Medicines, too numerous to mention, have been tried, with indifferent success in most instances; elaborate claims have been made for a few. Among the substances which seem to have had value in selected cases are tincture of iodine, gentian violet, and arsenic. Freshly-made tincture of iodine is given on a full stomach, in doses of from 5 to 15 drops in a glass of water three times a day. If improvement is not noted in the first week, administration should be stopped. Gentian violet can be prescribed in tablets of 0.03 gm. ( $\frac{1}{2}$  grain), and enough should be taken to colour the stools blue. Arsenic is a dangerous drug, and if it is given in the stage of active bleeding, the likelihood of its causing increased trouble and at times fulminating disease, is great. Once this happens it is difficult to do much for the patient. Since the wide publicity given to the outbreak of amoebic colitis in America in 1933, there has been a tendency toward indiscriminate use of arsenical preparations for many types of dysentery. This has worked to the detriment of some patients who had chronic ulcerative colitis. Arsenic, in a form such as P-carbamino-phenyl arsenic acid (carbarsone), or stovarsol, if used at all, should be used in small quantities and only as a tonic in the stage of improvement, and when active bleeding has stopped.

Mercurochrome and metaphen have been given by various observers, but results in our experience, from use of these drugs, have been indifferent.

Insoluble powders such as bismuth, tribasic calcium phosphate, and finer grades of kaolin are helpful in thickening the intestinal content, and at times in reducing the number of discharges. Of the first two, 4 to 8 gm. (1 or 2 drachms) can be given three to five times in twenty-four hours. Kaolin, 30 to 90 gm. (1 to 3 ounces) can be given with the same frequency.

As is the case in so many conditions, some form of opium or codeine serves a most useful purpose here. Camphorated tincture of opium in doses of 1 drachm (4 c.c.), the deodorized tincture of opium, in doses of 5 to 15 minims, codeine, in doses of  $\frac{1}{2}$  to 1 grain (0.03 to 0.06 gm.), quiet peristalsis, allay cramps, and in this way probably assist healing. We use these drugs very sparingly.

(6) The value of blood transfusions in some of these cases is inestimable. Blood may be given for two reasons: (1) in cases of severe sepsis and depletion to fight the toxæmia; (2) for anæmia and the weakness following loss of blood. Two to five transfusions, of 150 to 250 c.c. each, have much greater value than has one



transfusion, or more than one, of 500 c.c. or thereabouts. The transfusions of small amounts should be given at intervals of from four to seven days.

A suggestion recently made for treatment of this disease, although employed with indifferent success for other conditions, is the so-called immune transfusion. For this, the donor receives injections of a bacterin prepared from the diplostreptococcus of colitis, procured from the patient, for some time prior to the transfusion. Some physicians claim unusually favourable response from this procedure.

(7) Great bodily depletion occurs in this condition. Physiotherapy—including mild baking, and massage of aching limbs or back—and hydrotherapy, in the form of tepid baths and sponges, are very soothing. Sun-baths, systematically employed, have value. Administration of fluids, intravenously and subcutaneously, and transfusions of blood, have been mentioned. Cardiac stimulants are occasionally required.

(8) My experience, and that of many other clinicians, is that the good which may be accomplished by the so-called disinfecting irrigations is offset by the irritation they cause. The essential thing to be remembered is that no matter how powerful a disinfectant is used, one cannot hope, by giving it as an enema, to eradicate the infection. The disease extends deeply through all the layers of the bowel, and at times into the mesentery and even into the blood-stream. Consequently, the most that is accomplished by intestinal irrigation is cleansing of the surface, and that only for a few minutes. In cases in which there is much peri-anal infection, as there is in cases of fistula, irrigating the rectum with warm physiologic saline solution has given comfort. In those few cases in which such irrigations seem indicated, physiologic saline solution offers as much as, or more than, silver nitrate, mild silver-protein, acriflavine, or any of the many other solutions proposed from time to time.

In cases in which the disease is confined to the rectum and sigmoid, instillations of powders such as bismuth, of hamamelis (witch-hazel), or of silica jel, seem to have an added advantage.

(9) Demonstrable or accessible foci of infection should be removed, if possible, for they may serve as depots from which infection of the bowel may arise. Teeth with peri-apical abscesses, and suspicious-looking or definitely infected tonsils should be removed. The tender and inflamed rectal wall will usually prevent the massage necessary to clear up prostatitis. Peri-anal infections, cryptitis, and papillitis should be treated cautiously. In general it can be said that foci of infection should be removed in the stage of remission, or at least quiescence, of the disease.

Even though the active symptoms of the disease may have subsided, a patient must not relax in vigilance. If vigilance is maintained results may be excellent. Again it may be said that there is analogy between the course of this disease and tuberculosis, and every patient who has had a severe attack of ulcerative colitis is a potential colitis patient. Relapses are common if these matters are not borne in mind. The most common causes of relapse are: (1) Infection of the upper part of the respiratory tract, (2) mental and physical trauma, and (3) the lighting up of distant foci of infection.

#### RECAPITULATION

I have attempted to review the results of about fifteen years of rather intensive study of the disease, chronic ulcerative colitis, also known as colitis gravis, and perhaps better called thrombo-ulcerative colitis. Much of what I have said to-day I have expressed before, but since this is a review, rather than a report, of previously unpublished data, I hope you will not object to that. In the past fifteen years my own ideas and those of many of my colleagues, concerning the aetiology, pathology and treatment of chronic ulcerative colitis have undergone a great deal of change, and I hope and believe that these changes have resulted in benefit to the patient.

*Discussion.*—Mr. J. P. LOCKHART-MUMMERY said that the disease was of extraordinary severity in young people; very few sufferers below the age of 18 years survived. Dr. Bargaen had had one or two of that age-period who recovered, but his own experience with the disease in young children had been very unfortunate, no matter what was done and whatever diet was given.

He was glad that Dr. Bargaen insisted on a nourishing diet in these cases, because—some years ago—these patients were frequently put on starvation diet, and went from bad to worse. At St. Mark's Hospital, these patients were put on to as full a diet as they could take. A serious complication was stricture following ulceration, not immediately, but some years later. He had one patient, aged 65, who had ulcerated colitis for twenty-two years. The sigmoidoscope showed no ulceration, but a stricture in the rectum. X-ray revealed three or four bad strictures, the worst of which was  $3\frac{1}{2}$  in. long. She was passing from twenty to thirty stools a day. Complete colectomy seemed to be the only course, and under some circumstances that seemed scarcely possible.

Dr. P. H. MANSON-BAHR said he agreed with all the points which Dr. Bargaen had made, except as to the specificity of the diplococcus as the main cause of the disease. He himself considered that ulcerative colitis was not so much the expression of a direct infection of the intestinal tract, as the result of the excretion of some toxic substance from the body *via* the intestinal tract; he regarded it primarily as an allergic manifestation. There were superficial resemblances between the pathological appearances of bacillary dysentery and ulcerative colitis; but because pathological process produced the same appearance in the large intestine, it did not prove that these two diseases were ætiologically the same. In fact there was overwhelming proof that they were distinct.

He had recently made an analysis of all the dysenteriform cases which he had investigated and treated at the Hospital for Tropical Diseases during the last sixteen years.

There were 735 cases labelled "dysentery" or "colitis" from the tropics. 40 (5.4%) were cases of ulcerative colitis (colitis gravis); 484 (65.9%) were cases of proven amœbic dysentery; 121 (16.4%) were cases of chronic bacillary dysentery diagnosed by sigmoidoscopy and by the agglutination test; 66 (8.9%) were colitis secondary to amœbic dysentery; 24 (3.2%) were colitis secondary to bacillary dysentery.

There was no evidence that the cases labelled "ulcerative colitis" were connected with, or secondary to, any of the other forms of dysentery. Ulcerative colitis (colitis gravis) developed in susceptible people in the tropics just as it did in temperate countries; it had a distinctive course and symptomatology. The age-incidence appeared to be much the same, the disease being most frequent between the ages of 20 and 25. The eldest patient was 48. It was three times commoner in females than in males.

The sigmoidoscopic appearances were distinctive and he recognized in the living mucosa four out of the five stages of this disease described by Bargaen. Ulceration was follicular, destructive and terminal. The ulcerative stage marked the fully developed disease and might be produced by secondary organisms. Of the 40 cases, six were originally classified, on account of the localization of the process as "granular rectitis", as described by Milligan. Of these, half had afterwards developed into true cases of ulcerative colitis.

The mental attitude towards the disease was very important. In some persons it almost seemed to be of determinative value.

At present no specific treatment existed. Diet should be liberal; any attempt to restrict it caused an exacerbation. The one therapeutic measure which had definite curative value was blood transfusion repeated at short intervals in quantities of 200-300 c.c.

Transfusions which were followed by rigors, or general reactions gave the best results. Drugs were not of any value except in the treatment of urgent symptoms as they arose. He entirely disbelieved in large enemata. The best results were obtained by the injection of bland substances, such as olive oil (6 oz.) containing 5% bismuth subgallate, and rivanol (diamino-acridine-lactate) which was soothing and anti-spasmodic. It should be given in small retention-enemata 1 : 2,000 - 1 : 500 of from two to four ounces each.

Operative measures were only needed under special circumstances, and he had had experiences of about nine cases of cœcostomy and ileostomy in which the patient's life had been saved and health restored by those methods. In certain cases the best results were obtained by ileostomy, but no attempt could subsequently be made to close the opening as stenosis of the large intestine inevitably supervened in such an isolated and diseased bowel.

Mr. RALPH MARNHAM said that he had collected figures from nine London teaching hospitals, including all in-patients, from 1925 to 1929. In most of these the diagnosis was made by the sigmoidoscope or X-rays, a few by signs and symptoms alone.

No. of cases	Age			
	Average	Oldest	Youngest	
214 (M. 30%, F. 70%)	35	65	13	
Died in hospital	Left hospital	Traced		
67 (32%)	147	120 (84%)		
	Died	I.S.Q.	Recurrences	Cured
130 given medical treatment	40%	11%	40%	9%
84 given surgical treatment	44%	9.5%	37%	9.5%
120 traced ...	25 (21%)	11 (9%)	57 (48%)	27 (22%)
Total mortality of traced cases, 49.2%.				

The results were the same whether the patient was treated medically or surgically. Medical treatment of the cases included colonic lavage with a large variety of substances, zinc ionization, serum and vaccines, and various diets. The type of treatment seemed to depend on the hospital attended rather than on the stage of the disease.

He agreed with practically all that Dr. Bergen had said as to the uselessness of colonic lavage; to many patients it was detrimental. He thought that treatment by diet and appropriate serums offered the best chance of cure.

At St. George's Hospital there were two cases on whom cæcostomy had been performed without producing improvement. Transverse ileostomy—in one case followed by a complete colectomy—had resulted in the patients living happier and more normal lives than they had done for many years. If surgical treatment was necessary this operation seemed to be the kind indicated.

Dr. L. P. GARROD said that no speaker subsequent to the opener had referred to Dr. Bergen's own form of treatment, namely, the use of serum prepared by immunizing horses with a coccus which he had first described. This meeting would be incomplete without some further reference to that treatment, and the theories on which it rested. Dr. Bergen would be familiar with the fact that Paulson held a view which was severely critical of his hypothesis; he said that the characters of the streptococcus described by Dr. Bergen were not constant, and that he had been able to isolate a variety of cocci by methods used by Dr. Bergen, and some of these which were not definitely the same would produce colitis when injected into rabbits, as indeed would other bacteria not related to colitis. He (Dr. Garrod) would like to place on record the fact that though at one time he had had an open mind on this subject, he could not now accept the belief that this streptodiplococcus caused colitis. He had frequently found it in normal stools, and once in a case of bacillary dysentery. He therefore thought that, on the purely laboratory side, something was to be urged against what Dr. Bergen had said about aetiology, and in consequence about treatment. When he classified necessary treatment under nine headings, and added even an optimistic attitude on the part of the physician—as a condition necessary to success—one could scarcely attribute his own success in treating this disease to the innovation for which he was responsible. Since Dr. Bergen had so many cases under his care, it might be possible for him to introduce a series of controls, as by giving some of the patients normal horse serum.

Finally, he asked why Dr. Bergen sometimes gave his serum intravenously, as the only difference in the specific effect as compared with that of intramuscular injection was a slower absorption in the latter case. In a disease in which time was no object, this difference could have no importance, and the shock-like effect which might be secured by the intravenous route could be its only recommendation. Such an effect was entirely non-specific.

Dr. JULIUS BURNFORD said that so many forms of treatment had been put forward for ulcerative colitis, that little advance had been made beyond ventilating the various types of treatment. Proof of cure by a serum should be more obvious and more readily ascertainable than proof of cure by other remedies. Serum, if specific, should produce specific results, yet, as Dr. Garrod had said, there did not seem to be evidence that particular serum was more specific in its results than any other treatment. The fact was that this terrible disease could even at the present time be described almost as incurable. He himself had

had 150 cases of ulcerative colitis in twenty years, and he considered that it was becoming more frequent, though diagnosis was now better.

Many years ago he had brought to the notice of the Society a line of treatment which, in his early enthusiasm, he had regarded as the only hopeful one for this disease, namely, that by zinc ionization. The results in his first twenty-eight cases, particulars of which he had published, were very stimulating. But recent cases which he had seen were much more serious, and only occasionally did zinc ionization bring benefit.

He had then changed the diet of his patients, and it was interesting to him to hear Mr. Lockhart-Mummery agreeing with Dr. Bargaen that a full diet was essential for the successful treatment in these cases. Even now he had patients, transferred from other hospitals, who were little more than shadows, this condition having been brought about by a purely milk diet. He allowed his ulcerative colitis patient all they wished to eat, and he did not even consider the character of "roughage" in the diet, as he held that in order to stimulate and bring back the normal functions of the large bowel it was necessary for it to contain, not a stinking mass of fermenting material, but soft pulpy material. That could do nothing but good. Starchy foods only were restricted, in order to diminish fermentation. In the last few months he had had extraordinary results in two cases. One patient who had wasted a great deal had been operated upon—it was thought for perforation—but the cæcum had been found not affected. Intubation had then been carried out by Mr. Simpson-Smith, and oxygen had been passed through the tube continuously for four weeks. That patient was now back at work, wearing the tube; he had put on seven stone in weight, and was now in good condition. Though he had polyposis, he passed a normal stool. In St. Mary Abbots Hospital was a girl who had been practically moribund when brought in. The same procedure was carried out in her case, and she went out in normal health.

Mr. R. S. CORBETT described two cases which had been treated this year at St. Bartholomew's Hospital for this condition by terminal ileostomy.

The first was that of a woman aged 22. She had had appendicostomy, and after leaving hospital she had apparently improved, but a cæcostomy occurred spontaneously, she came back very ill, and her weight was only four stone. She was completely bedridden, and lay continuously on a bedpan. Dr. Graham had persuaded him (the speaker) to perform ileostomy, and he had been encouraged to do so by Dr. Manson-Bahr's case. Within six weeks of the operation the patient had doubled her weight, and was now leading a normal life, and did not seem to be upset by the operation.

The other patient was a woman, aged 36, who had had trouble two years; there had not been previous appendicostomy or cæcostomy, but she was very ill. She had repeated hæmorrhages, which could not be controlled and therefore it was considered justifiable to perform a terminal ileostomy. Unfortunately the patient died on the twenty-fourth day after the operation, from bilateral bronchopneumonia, which led to an empyema. Post-mortem examination showed that the ulceration of the bowel, which had reached the third stage, had almost completely disappeared. There was only one area in the large bowel which showed ulceration, and but for the pneumonic complication the operation would have been a complete success.

Dr. BARGEN (in reply) said he felt definitely that the last word had not been said or written on the ætiology of chronic ulcerative colitis. There could be other bacteria which helped to constitute the well-known picture of this disease, yet he was practically certain that the particular type of streptococcus he had mentioned was the inciting factor, whatever else might complicate or modify the condition. There were many predisposing factors in any infectious disease. He thought, therefore, that there was ample justification for carrying on treatment as outlined, until someone came along and added substantial improvements. Neither could it be alleged, that the last word on treatment had been said, but in the last few years something had been evolved which suggested that important forward strides were being made. There was, he thought, no justification for placing mild cases into different groups. He had seen patients with colitis stay in the mild condition for a long time and then suddenly, without apparent reason, progress into the severe phase. All the cases should be treated as if they constituted a part of the same picture, and according to the definite programme outlined. To adopt the best means of helping these unfortunate patients, was more important than everything else, and therefore much energy should be exerted on the clinical side.