

## Original Articles

## CHRONIC ULCERATIVE COLITIS

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THE problem of ulcerative colitis remains unsolved; medical opinion has oscillated between the extremes of optimism and pessimism. There are some, notably Bergen (1935) and Buie (1937), who would class it among the conquered diseases, while others, Hetenyi (1935) for instance, would classify it equally emphatically among the incurable diseases. The significance of such startling divergence of authoritative opinion will be missed unless we take into consideration the geographical distribution of the disease and the changes in dietetics and habits, induced by the complexities of modern civilization. The consensus of medical opinion is more inclined to regard it in the same light as pulmonary tuberculosis; the disease can only be arrested by prolonged treatment, involving rest in bed and maintenance of mental peace. Spontaneous intermissions are not uncommon, but intercurrent infections and emotional disturbances have marked deleterious effects on the progress of the disease.

This paper is based on the study and statistical survey of 120 cases of ulcerative colitis under our care in the Medical College Hospitals and the Carmichael Hospital for Tropical Diseases. The present investigation was undertaken as a supplement to our previous work on 'Amoebiasis and Appendicitis' (Banerji, Chopra and Ray, 1936), wherein it was observed that the incidence of non-specific colitis in a small series of cases for sigmoidoscopy was as high as 43 per cent.

**Definition.**—Chronic ulcerative colitis may be regarded as a disease of the large intestines during the second and third decades of life with characteristic clinical and pathological features but without any specific bacteriological infection.

The effects of allergy, avitaminosis, faulty body mechanics and emotional disturbances have yet to be precisely determined. The view that, like peptic ulcer, it may be a local manifestation of a general disease has much to recommend it but requires confirmation.

*Ætiology*

There is still considerable confusion in the description of ulcerative colitis. From available evidence, it appears that in a variable percentage of cases no bacteriological relationship can be

established. Neither is there any unanimity of opinion regarding the ætiological factors, although it is customary to refer to various predisposing causes. We shall therefore briefly discuss the present position.

1. *Bacillary dysentery.*—Chronic ulcerative colitis has often been regarded as a sequela to bacillary dysentery. Penner (1936) is of opinion that, in the tropics, a large percentage of cases belongs to this category, while Hurst (1931) strongly advocated the use of antidysenteric serum. Our experience does not seem to confirm this view (Chopra, Hayter and Bhattacharya, 1937). It is a curious fact that children appear to be immune from ulcerative colitis, although they are known to suffer from bacillary dysentery and its usual terminal complications (Ray, 1934).

2. *Amoebic dysentery.*—*Entamoeba histolytica* has also been regarded as a causative agent, but this view has not been confirmed by laboratory and other evidence.

3. *Streptococcal infection.*—In recent years, much attention has been paid to the investigation of a possible bacterial origin of chronic ulcerative colitis. Bergen (1935) is of opinion that a diplococcus, isolated by him from ulcers of the colon, is the cause of the disease. Intravenous injections of Bergen's diplococcus in the rabbit are said to produce diarrhoea with blood and mucus, but it cannot be said that the experimental disease bears any resemblance to the chronic ulcerative colitis in man. It is, however, important to note that this disease is prone to occur in association with infections of the upper respiratory tracts, e.g., coryza, tonsillitis, recurrent pharyngitis, and sinusitis. Influenza would seem to require special mention. The incidence of streptococcal infection in ulcerative colitis has varied within wide limits in the hands of different workers. There is no doubt of a streptococcal relationship in some cases although the question has yet to be answered, whether the infection is primary or secondary. In our hands the figures are far from convincing. The empirical administration of 'Prontosil' and anti-streptococcal serum in a number of control cases has not been marked with any tangible success.

4. *Avitaminosis.*—There is little doubt that persistent deficiency of vitamin C in the diet is an important predisposing factor in the causation of recurrent hæmorrhages from the bowel in case of chronic ulceration of the colon. In a few cases we have obtained very satisfactory results with the administration of vitamin C ('Cantan', Bayer). Uniformly good results have also been reported by Hetenyi (1935). Familiarity with the beneficial effects of cod-liver oil as a local application in various kinds of ulceration led us to try it as a local instillation in ulcerative colitis. The result was a pleasant surprise. Similar results have also been reported by Spiegel (1937) and the improvement is ascribed to the presence of vitamins A and D. We cannot exclude a reference to the vitamin-B

complex. As a dietary adjunct in the treatment of ulcerative colitis, it is generally indicated and for this purpose 'marmite' has given consistently good results. In spite of accumulated evidence, it is not yet justifiable to include ulcerative colitis in the group of the 'deficiency diseases'.

5. *Allergy*.—The question of allergy cannot be dismissed without careful consideration. In about 20 per cent of cases a positive history of allergy with regard to some specific foodstuff is obtained, and here 'Torantil' (Bayer) has been found to be of use. In two cases, the remarkable history was obtained that an improvement of the colitis was invariably noticed with the appearance of eczematous patches on the body. In another case, the onset of bronchial asthma would definitely bring about an amelioration of symptoms. Chronic ulcerative colitis presents some features comparable to those of chronic eczema or neuro-dermatosis.

6. *Faulty body mechanics*.—Poor body mechanics may give rise to functional disturbances of the colon to which have been attributed a long list of ailments ranging from indigestion to neurasthenia, and from auto-intoxication to arthritis. The primary factors in the production of these symptoms are chronic passive congestion, stasis and disturbed innervation, which may be caused by the abnormal position of the internal organs always found in faulty posture (Goldthwait, Brown, Swain and Kuhn, 1937).

7. *Emotional disturbances: 'Tropical Neurasthenia'*.—It is a curious fact that exacerbations of chronic colitis are, in nearly 50 per cent of cases, associated with some previous emotional disturbances of a serious nature. The similarity of this aspect of the disease to peptic ulceration is worthy of note.

8. *Other causes*.—In a disease of unknown origin the list of probable causes cannot be easily exhausted. Intestinal parasites which are so common in tropical countries have also been blamed for more than one symptom. Irregularity of hours, unsuitable dietary, addiction to drugs, and smoking and enteritis following typhoid and other exanthems have all been regarded as possible exciting causes.

To sum up, we are constrained to state that we are unable to determine any single aetiological factor for ulcerative colitis. It is probable that many factors combine to produce devitalization of the mucous membrane of the large intestines leading to chronic ulceration.

#### Pathology

The pathological concept has gradually veered round to the position that the lesion is not restricted to the mucosa but involves the sub-mucosa and, in later stages, the muscular coats. Although the ulceration is usually confined to the large gut, in severe old-standing cases it may extend to the adjacent part of the ileum. The parts most involved are the rectum, sigmoid, and the caecum. The post-mortem appearances do

not give a correct idea of the disease, because the gross changes which are found in the later stages are considerably modified by the appearance of many complications and sequelæ.

*Macroscopic appearances*.—The naked-eye appearances of the mucous membrane may be carefully studied with the help of the sigmoidoscope. As the sigmoidoscopic appearances are characteristic, diagnosis is not difficult and, for convenience of clinical description, the lesions may be described in several stages. It is necessary to remember that, in the old-standing cases, these different stages cannot be strictly differentiated owing to considerable overlapping of signs, resulting from recurrent exacerbations. In the *first stage*, the mucous membrane of the rectum and the sigmoid colon shows signs of hyperæmia and inflammation (plate V, figure 1). The slightest trauma during instrumentation will give rise to bleeding. In the *second stage*, the œdematous mucosa, studded with numerous greyish-yellow granules, cannot be mistaken by the trained observer (plate V, figure 2). The transverse folds of the colon lose their sharp outline and become rounded and œdematous. The greyish-yellow granules represent minute necrotic foci or areas of degeneration under the unbroken lining epithelium. In the *third stage*, the greyish granules, having broken down, give rise to minute multiple ulcers producing a moth-eaten appearance to the mucous membrane (plate V, figure 3). The bleeding is due to the oozing from these ulcers and at times may occur in alarmingly large quantities. The *healing stage* will show multiple pale ulcers, which can only be described as indolent, and scattered scars (plate V, figure 4). In the more *chronic stage*, obliteration of the rectal valves, thickening of the mucosa, the presence of multiple granular vascular polyps and narrowing of the lumen, complete a characteristic picture (plate V, figure 4). There is another group of cases, in which large chronic ulcers are found scattered, showing little sign of healing (plate V, figure 5) owing to supervention of secondary infection from the contents of the alimentary tracts.

The *active or third stage* of chronic ulcerative colitis may assume a virulent form, characterized by severe pyrexia, widespread ulceration and marked prostration. It is necessary that in such cases great care should be exercised during sigmoidoscopic examination, otherwise there is danger of severe hæmorrhage or even perforation (plate V, figure 6). The lumen of the gut becomes markedly constricted and the friability of the soft tissues increases the dangers of instrumentation.

*Histological appearances*.—Owing to the protracted nature of the disease and absence of mortality in the early stages materials for histological study cannot be procured easily. The obvious difficulties of biopsy require no explanation; sections of the mucosa alone are not sufficient, and section through all the coats

of the large gut is a formidable procedure which cannot be lightly undertaken. Deaths during the early stages are usually due to other intercurrent diseases and, in the later stages, to various complications and sequelæ.

At an early stage of the disease, when the mucosa is inflamed but no ulcers have yet appeared, the microscopic picture consists of dilatation of the smallest capillaries, diapedesis and minute hæmorrhages. But the histological appearance of the granular non-ulcerated mucosa is very different and significant; it presents a homogeneous area with scanty cellular elements. There are pyramidal areas under the mucosa showing degenerative changes corresponding to occlusion or thrombosis of the deeper vessels.

This picture is considerably modified when sections are made through the moth-eaten granular mucosa, which reveal multiple miliary ulcers (plate VI, figure 7). The pin-head areas of degeneration or the miliary necrotic foci ultimately break down forming the characteristic chronic ulcers. These degenerated areas consist of hyaline material and are surrounded by some round-celled infiltration and fibrous tissue, sometimes very well marked, indicating the chronicity of the lesion (plate VI, figure 8). Similar changes are also found scattered throughout the different coats of the gut. The destruction of the lining epithelium appears to be gradual while the degenerative changes continue their steady course in the surrounding connective tissue (plate VI, figure 9). It is worthy of note that even fibrosis of these degenerated areas is a very slow and, probably, an incomplete process. Endarteritis obliterans is nowhere to be seen. The histological picture appears to be a very definite and characteristic entity, such as is seen in no other ulceration of the large intestines.

*Quiescent periods.*—In the intervals between the acute exacerbations of colitis, there are varying periods of intermission of symptoms. It is doubtful if the ulcers are completely healed during these periods. The analogy to duodenal ulceration is very close in this respect. The sigmoidoscopic appearance consists of pock-like scars, on a pale and 'glazed' mucosa. Microscopic sections will naturally show a variable amount of submucosal fibrosis.

*Ulcers due to secondary infection.*—It has already been pointed out that secondary ulcers usually supervene upon the miliary moth-eaten ulcers of chronic ulcerative colitis. These are caused by the invasion of the ulcerated area by the pathogenic organisms inhabiting the lower alimentary tract. In the very chronic cases, these secondary ulcers may be very widespread, causing a great deal of fibrosis and stenosis of the lumen. During the quiescent period, they may present the characters of superficial callous ulcers, but during an acute exacerbation, they may be transformed into deep penetrating or excavating ulcers, not infrequently simulating malignancy.

*Complications and sequelæ.*—With each acute exacerbation, the functions of the large intestines, *viz*, absorption of fluid and motility of peristalsis, are grossly interfered with. Owing to extension of ulceration, fibrosis of the muscular coats, and destruction of the lining epithelium, diarrhœa and mucous discharge may become intractable, making the patient a chronic invalid. Recurrent rectal hæmorrhage may endanger life and give rise to severe anæmia. The bleeding is usually bright red, but melæna is not uncommon, indicating bleeding from the cæcum and the proximal colon. Stenosis of the lumen is a constant feature of the chronic cases; when well marked the lower colon, and in particular the rectum, become converted into an unyielding narrow tube lined with chronic indolent ulcers, giving rise to purulent and hæmorrhagic discharge. The diagnosis of these cases may be very difficult. Perforation, adhesions, pericolicitis and fistulæ-in-ano may be regarded as other important sequelæ.

The extent and distribution of these pathological changes vary a great deal, and in cases operated upon it was found that all the coats of the colon were involved. The lymphatic glands in the mesentery and sigmoid mesocolon are invariably enlarged and œdema of the mesocolon is also common. It has not been possible to determine yet whether this is not due to a secondary infection. It is, however, worthy of note that the lymphatic nodules of the intestines, unlike those in typhoid fever, remain fairly healthy. Capillary thrombosis, hyaline degeneration and infarction appear to be the main histological lesions, but these findings are unknown in chronic colitis associated with bacillary dysentery and gummatous ulcers. It is somewhat difficult to explain the occurrence of such extensive ulceration as being wholly due to devitalization, resulting from impaired vascular supply. Such a widespread lesion, associated with endarteritis obliterans, is not even seen in course of syphilitic ulceration of the colon. The hæmorrhage is usually caused by the ulcers, but the so-called granular 'polyps', which are masses of granulation tissue, may at times be responsible. These are comparable to the nodules seen in epidemic dropsy.

#### *Bacteriology*

In the analysis of our cases we have not been able to point to any particular organism as the exciting cause. There is no evidence to show how the infective organisms invade so large an area of the gut. Even in the earlier stages, an extensive area of the gut is involved. There is no evidence to show that the disease is liable to appear at any particular region of the colon or to spread in any particular direction. In spite of every care in the majority of cases, no growth could be obtained on culture of the scrapings of ulcers. The bacterial examination of fæces may be found of interest in this connection.

TABLE I  
Microscopical examination of fæces in 100 cases

Helminths—		
<i>Trichuris trichiura</i> eggs ..	..	3
Hookworm eggs ..	..	8
Protozoa—		
<i>Giardia</i> cysts ..	..	5
<i>Entamoeba histolytica</i> —		
Vegetative forms only ..	..	1
Cysts only ..	..	2
Vegetative forms and cysts ..	..	1
Charcot-Leyden crystals ..	..	4

As ankylostomiasis is fairly widespread in this part of the country, its coincidence with ulcerative colitis is not significant.

Amœbic dysentery is common in India. A routine examination of the fæces of patients admitted into the Carmichael Hospital for Tropical Diseases showed an incidence of 12 per cent of infections with *E. histolytica* (Chopra, 1936). In the present series the incidence is only 4 per cent. These cases were treated for amœbiasis and the stools were examined repeatedly until they were negative for the parasite. The association of Charcot-Leyden crystals with amœbiasis does not appear to be of any significance.

TABLE II  
Cultural examination of fæces in 100 cases

Organisms	Present survey	Chopra, Hayter and Bhattacharya (1937)
<i>B. pseudo-carolinus</i> ..	14	20
<i>B. asiaticum</i> ..	11	5
<i>B. carolinus</i> ..	8	Nil
<i>Ps. pyocyanea</i> ..	7	5
<i>Strepto. faecalis</i> ..	4	1
<i>Bact. alkaligenes</i> ..	3	18
<i>B. pseudo-asiaticum</i> ..	3	3
<i>B. morgani</i> ..	2	5
<i>B. meta-alkaligenes</i> ..	2	1
<i>B. flexner</i> ..	2	Nil
<i>B. shiga</i> ..	1	Nil
Monilia ..	1	Nil

The incidence of bacillary dysentery was only 3 per cent and it compares very favourably with that of amœbiasis. The non-dysenteric character of chronic ulcerative colitis is therefore clearly indicated. *Streptococcus faecalis* was isolated in only 4 per cent of cases. We have included *Ps. pyocyanea*, *Bact. morgani*, *B. carolinus* and *B. meta-alkaligenes* in this investigation because there are good reasons for believing that they might cause intestinal disorder.

Scrapings from the ulcers of the rectum and sigmoid showed the presence of Gram-positive cocci on three occasions. Other organisms isolated were a Gram-positive spore-bearer, staphylococci, a Gram-positive bacillus, a Gram-negative bacillus, and diphtheroids on one occasion each; these findings indicate the non-specific character of these ulcers.

It would appear to be extraordinary that no better information could be obtained by careful examination and culture of the scrapings of these ulcers. It may be objected that the infection is deep seated and therefore no further information could be obtained from the scrapings of comparatively superficial tissues from the floor of the ulcers.

*Culture of blood.*—It was hoped that by adopting special measures a conclusive result might be obtained, but a positive bacterial finding was an exception rather than the general rule, and in only two out of twenty cases spore-bearing organisms were isolated after forty-eight hours. No pathogenic organisms were isolated.

#### Investigations and diagnosis

Cases of ulcerative colitis are generally treated as dysentery before any surgical advice is sought, consequently the early stage, which is the best for chances of recovery, is seldom seen by the surgeon. Much valuable time is usually lost by treatment for hypothetical parasitic infections. On an average we get a history of three or four years' recurrent attacks of indigestion, diarrhoea and dysentery with repeatedly negative stool reports. In these chronic cases a great deal of care and caution would be necessary because in about 26 per cent of cases there is a positive history of bacillary or amœbic dysentery within a period of five years. The sigmoidoscopic examination is usually conclusive for diagnosis and it may be stated as a general rule that the rectum and the sigmoid are never free from the characteristic ulceration. In each case, provided there is no bleeding, further information may be obtained by skiagraphy after an opaque enema.

*Sigmoidoscopy.*—A careful digital examination is always necessary before instrumentation. Much valuable information is obtained with regard to the condition of the sphincters, the calibre of the lumen, and degree of severity of pain. No violence is permissible and it is always important to keep in mind the friability of the mucosa, owing to its inflamed condition and its liability to hæmorrhage. No local anaesthesia is generally necessary and no special preparation other than a saline enema on the previous night is called for. A sigmoidoscope with a smaller calibre is preferable as in the majority of cases there is some narrowing of the lumen.

TABLE III  
Analysis of sigmoidoscopy

Lesions	Percentage
Mucosal thickening and congestion ..	17
Miliary ulcers (moth-eaten) ..	38
Large ulcers with grey base ..	6
Ulcers with gelatinous matter ..	6
Multiple minute bleeding points ..	7
Red granular polyps ..	7
Scars of healed ulcers ..	7
Narrowing of lumen: stenosis ..	6
Fissures ..	2
Fistulae ..	2

The sigmoidoscopic appearance of these ulcers and their different stages have already been described. A differential diagnosis, however, must be made from amœbic ulceration.

During the early stages of the disease, spasticity of the gut was usual; the descending colon (in 35 per cent) and the ascending colon (in 31 per cent) were almost equally involved. In 10

TABLE IV  
*Differentiation from amœbic ulceration.*

	Amœbic ulcers	Ulcerative colitis
Nodules .. ..	Over crests of transverse folds.	Miliary granules, so-called 'polyps'.
Ulcers .. ..	'Button-hole' undermined and shaggy.	Pin-head and pock-like moth-eaten appearance.
Scars .. ..	Oval or rounded central pigmentation.	Pock-like.
Rectal valves and folds	Some thickening but folds present.	Obliteration of the valves, œdema of mucosa.
Scrapings .. ..	Viscid gelatinous.	Friable and bleeding.

*Sterile swabs and culture of scrapings.*—These procedures are carried out as routine measures and have already been described.

*X-ray examinations and opaque enemata.*—Skiagraphy should follow sigmoidoscopy; a barium meal is usually given in order to investigate the condition of the gastro-intestinal tract. From a radiological survey of our cases in this series, we find that some abnormality of the duodenal cap is present in 37 per cent, a 5-hour residue in the stomach in 28 per cent and other gastric anomalies in about 5 per cent of the total number of cases. An explanation of the gastric symptoms is thus readily obtained, the gastric residue is due either to pyloro-spasm or to atony. There was only one case of duodenal ulcer, the remainder came under the heading of duodenitis (plate VIII, figure 10).

TABLE V  
*Analysis of 120 cases of colitis : a radiological survey*

Stomach—			
5-hour residue .. ..	..	..	28
Other anomalies .. ..	..	..	5
Duodenum abnormalities of cap ..	..	..	37
Appendix—			
Visualized .. ..	..	..	33
Residue .. ..	..	..	3
Cæcum abnormalities .. ..	..	..	17
Ptoisis .. ..	..	..	20

The appendix was visualized in 33 per cent of cases while a residue was obtained in 3 per cent only. From the study of these figures it appears that gross lesions did not extend, at the earlier stages, throughout the entire length of the large gut. Abnormalities of the cæcum were present in 17 per cent.

TABLE VI  
*Analysis of the radiological appearance of the colon*

	Spasticity	Dilatation and stasis
Ascending colon .. ..	31	18
Transverse colon .. ..	5	5
Descending colon .. ..	35	5
Hypermotility .. ..	10	..
Irregular filling .. ..	20	..
48-hour residue .. ..	28	..

per cent of cases, there was hypermotility associated with diarrhœa. The descending colon appears to be more liable to stenosis with permanent narrowing of the lumen (plate VII, figure 11). Dilatation of the ascending colon was present in 18 per cent and of the descending colon in 5 per cent. A 48-hour residue was obtained in 28 per cent, representing chronic cases with ulceration and narrowing of the lumen (plate VII, figure 12). It is evident that skiagraphy will reveal the extent of the disease, site of stenosis, fixity of the gut and loss of haustration (plate VII, figure 13). Some malformation of the cæcal base is also an important feature.

*Clinical features*

*Incidence of sex.*—The percentage ratio between males and females was 72 : 28.

*Incidence of age.*—Chronic ulcerative colitis is chiefly a disease of the second and third decades of life.

*Early stage.*—The clinical features in the early stages are unfortunately not very definite and the condition is generally diagnosed as dyspepsia, 'tropical neurasthenia', chronic constipation, recurrent diarrhœa, or even dysentery. But when the signs and symptoms are well marked, diarrhœa, precipitate motions, with discharge of mucus and blood are prominent features. In spite of periodic remissions vague digestive symptoms are generally complained of. The incidence of gastric symptoms is easily explained by a reference to the tables on radiological analysis. The rarity of the presence of peptic ulceration is worthy of note. In general, abdominal cramps, rectal pain and discomfort, tenesmus and urgency may make life unbearable. Pyrexia is present at some stage or other in nearly half the cases. The pulse is an important guide to prognosis for, if it exceeds 120 per minute, it is a serious omen (Bell, 1936). In this review, we are not considering the acute type of ulcerative colitis which quickly leads to a fatal termination.

*Periods of remission.*—These are very variable but each succeeding attack becomes more acute than the last one and brings about severe prostration and loss of weight. Many of these cases are considered to be 'tropical neurasthenia', because the condition is frequently ushered in by serious emotional disturbances. Relapses are

common after infections of the upper respiratory tract.

*Intestinal hæmorrhage.*—The incidence of hæmorrhage is also variable. In one attack it may be alarming and in the succeeding ones there may be no bleeding at all. The blood may be bright red and may come with frequent discharge of mucus, but melæna is not uncommon when the cæcum and the proximal part of the colon are involved.

*Clinical types.*—It is not always possible to divide chronic ulcerative colitis into clinical types but it would be of some practical use to consider them as belonging to one or other of the following groups: (i) infective, (ii) allergic, (iii) avitaminotic, and (iv) neurasthenic. These will be referred to in the next section.

#### Treatment

It has to be admitted that there is no specific for this condition; the treatment is generally protracted and somewhat onerous, a careful dietetic regime having to be maintained.

I. *General and medical treatment.*—As early cases are seldom seen by the surgeon, only chronic and moderately serious cases are included under this group. The time of strenuous treatment is at the early stages before the colon is converted into a physiologically inefficient organ owing to fibrosis and stenosis (Goodall, 1936).

1. *Rest in bed.*—This is very important for maintenance of strength and control of fever. Exercise or activity usually increases the tenesmus and frequency of motions. *Postural treatment.* In the more serious cases, frequency of motions is distressingly increased even by the erect posture alone. Appreciable relief is quickly obtained by beginning the treatment in the recumbent position. In this position the force of gravity, which increases the sag of the organs and the strain on the body as a whole when in the upright posture, is practically eliminated. For this purpose both the 'hyperextension position' with dorsal decubitus and pillows under the knees, and 'the face prone' position are recommended.

2. *Diet.*—By general consensus of opinion a low-residue diet is best, but it is important to remember two fundamental desiderata. Firstly, the diet should be made up of adequate calories for maintenance of good health and body-weight, and, secondly, it must contain the necessary vitamins. Many patients go down hill because the diet is too restricted and monotonous. In a case of moderate severity it is best to begin with a modified Sippy treatment with addition of Benger's food and suitable extractives. A more generous diet may be quickly allowed, provided there is no bleeding or abdominal cramps.

3. *Administration of vitamins.*—There is reason to believe that avitaminosis is an important factor in the ætiology of this disease. (i) Ascorbic acid (vitamin C) has an excellent styptic effect in hæmorrhages of ulcerative colitis.

It is given in the form of 'Cantan' (Bayer) either intravenously or intramuscularly in daily doses of 150 mgm., until there is only one motion free from blood and pus (Hetenyi, 1935). In less urgent cases the drug may be given orally, the usual dose being one tablet three times daily. (ii) *Vitamin-B complex.* It is as yet difficult to indicate the precise effect of vitamin-B complex on ulcerative colitis. In the form of 'marmite' it has been found to be a valuable adjunct in the treatment of this disease. (iii) *Vitamins A and D.* We cannot say that cod-liver oil by mouth has been beneficial but rectal instillation has been attended with gratifying results and will be referred to again.

4. *Treatment of allergy.*—There is little doubt that in a number of cases a definite history of allergy is obtained, but it is not possible to state at present whether the allergy is due to a particular protein or some unknown amino-acids as the result of incomplete digestion. In this group 'Torantil' (Bayer) is worthy of trial as very gratifying results are not infrequently obtained. One ampoule of 'Torantil' is injected intramuscularly twice a week; one course comprises five injections. This is followed by a course of oral treatment consisting of one pellet before each principal meal for one week. The patient should be watched carefully as in some cases, which are impossible to predict, the symptoms may be definitely aggravated. In one case, after the ingestion of two pellets, serious bleeding was definitely stopped.

5. *Mental tranquillity.*—The restoration of mental peace after serious emotional disturbance is not easily achieved. In these cases it may be necessary to administer sedatives. Elimination of mental worries tends to rapid improvement in one group of cases which may be called the neurasthenic type. Vitamin-B complex is usually beneficial in this type of case. Psychotherapy may be needed in a serious case of nervous breakdown and severe mental depression.

6. *Vaccines and sera.*—Bargen (1935) and Buie (1937) report excellent results with auto-vaccines and specially prepared sera, but we have not been very fortunate in our results. 'Pron-tosil' (Bayer), which has been so successful in our hands (Ray, Alam and Ghose, 1938) in

#### EXPLANATION OF PLATE V

Fig. 1.—The mucous membrane of the rectum and the sigmoid colon shows signs of hyperæmia and inflammation (first stage).

Fig. 2.—The oedematous mucosa is studded with numerous greyish-yellow granules (second stage).

Fig. 3.—Showing minute multiple ulcers; 'moth-eaten appearance', old scars and a small vascular polyp (third stage).

Fig. 4.—Showing multiple pale ulcers and some granulating ulcers with marked tendency to bleeding (healing stage).

Fig. 5.—Showing a large chronic ulcer, with little sign of healing, owing to superelevation of secondary infection.

Fig. 6.—Showing a very acute type of ulceration.

PLATE V



Fig. 1.



Fig. 2.



Fig. 3.



Fig. 4.



Fig. 5.



Fig. 6.

PLATE VI

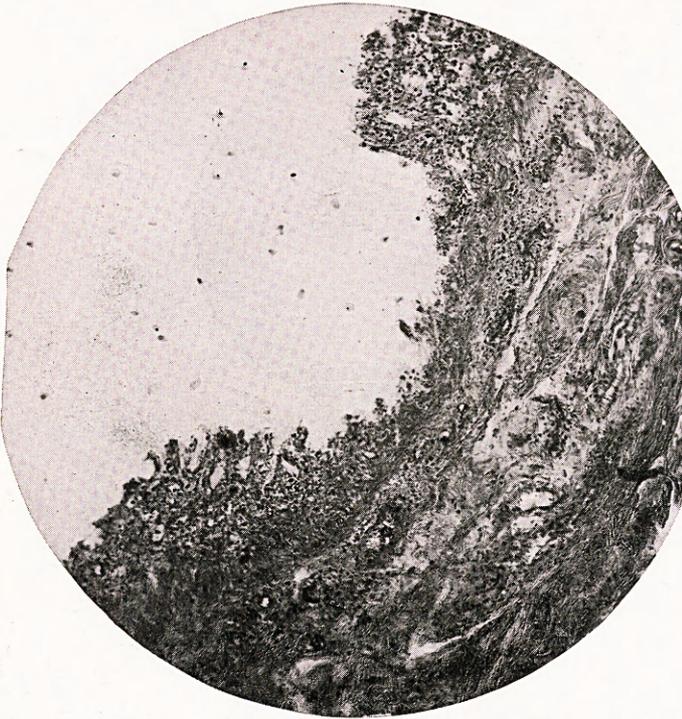


Fig. 7.—Section through one of the miliary ulcers of 'the moth-eaten granular mucosa' showing thrombosis of deeper vessels, scattered hyaline degeneration and fibrosis.

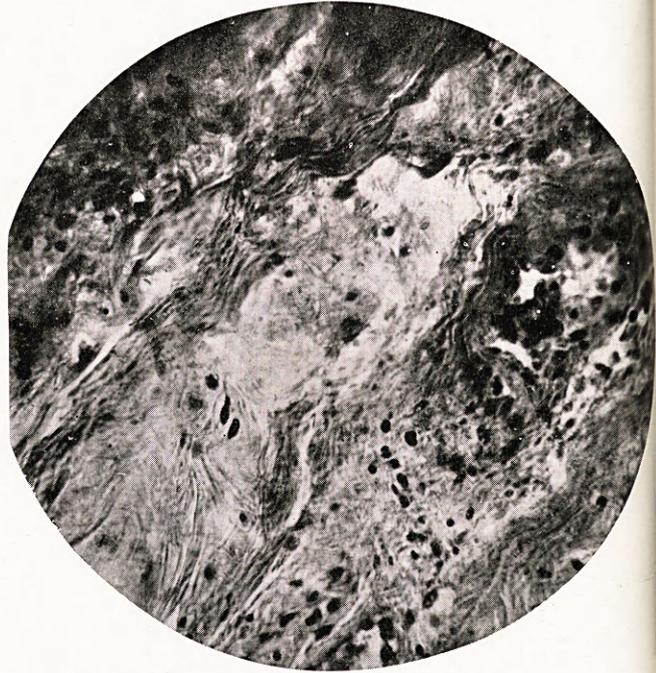


Fig. 8.—Photomicrograph through an area of degeneration containing hyaline substance, surrounded by well-marked fibrosis. (Zeiss 1/6  $\times$  2.)

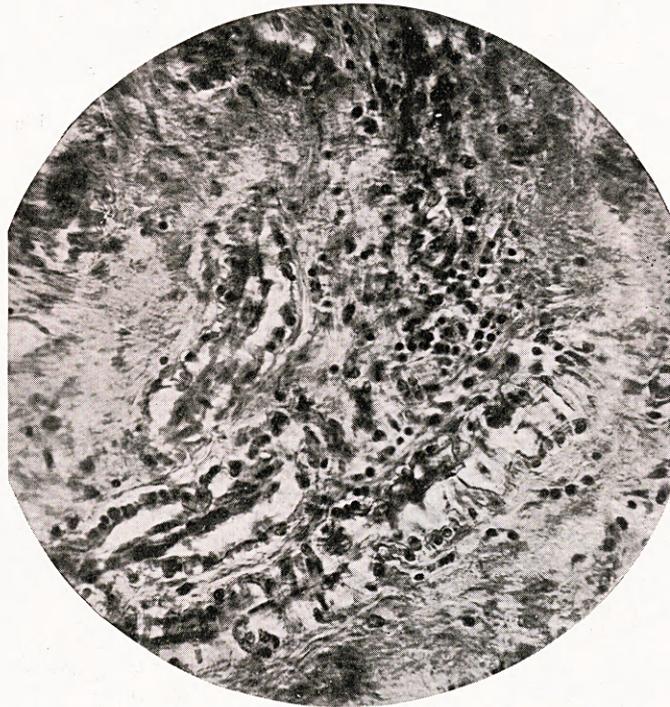


Fig. 9.—Photomicrograph. Section through the mucosa, showing degenerative changes around the glandular acini. (Zeiss 1/6  $\times$  2.)

PLATE VII

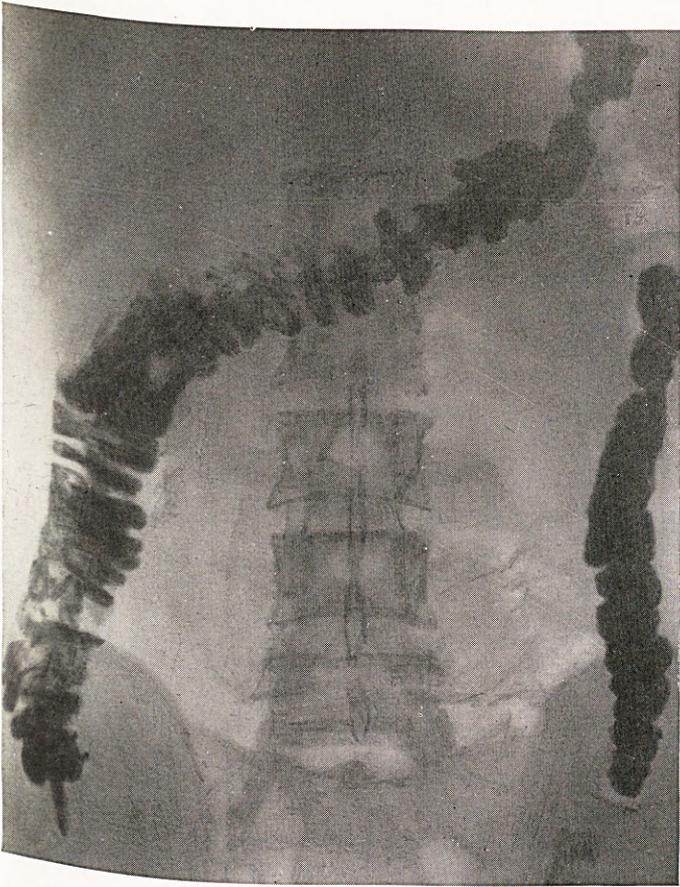


Fig. 11.—Showing poor haustration of the descending colon.



Fig. 12.—Showing 48 hours residue in the transverse colon.

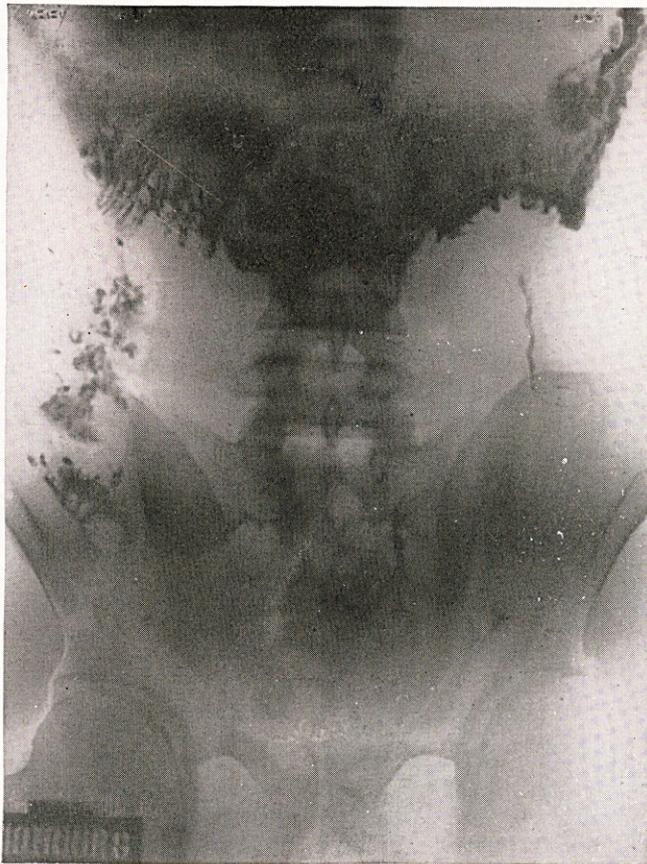


Fig. 13.—Note the 'string sign' of colitis, descending colon. Caecum has emptied rapidly, leaving flakes behind.

PLATE VIII

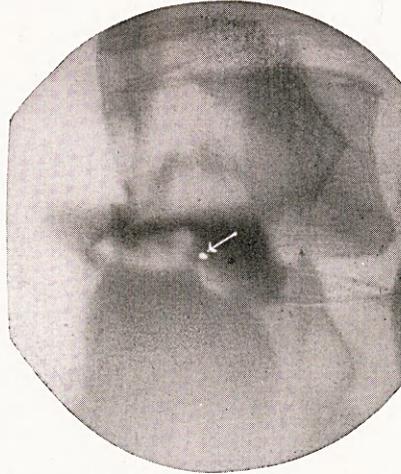


Fig. 10.—Showing some deformity of the duodenal cap.  
Suspected duodenitis.

Aberrant Pancreatic Tissue in the Alimentary Tract:  
Lieut.-Col. M. M. Cruickshank.



Fig. 1.



Fig. 2.

Sections of tumour removed from jejunum.

various streptococcal infections, does not seem to be efficacious; neither have anti-streptococcal sera of reputable makes proved of any greater value. Auto-vaccines in a few cases have been beneficial, affording some amelioration of symptoms.

7. *Drugs.*—There are no specific drugs, but a few need mention for purposes of symptomatic treatment :—

(i) *Buffered citrate therapy* (Montague, 1934). Success has been claimed with this method of treatment and it is ascribed to an improvement of acid-base balance of blood, lessened tendency to alimentary capillary stasis and venous thrombosis, and improved tissue resistance to general infection. Schultz's solution is used for intravenous injection. It consists of a combination of sodium citrate and sodium chloride buffered with a salt which raises the concentration of the solution somewhat higher than that of normal blood. The initial dose consists of 10 c.cm. This is doubled after 24 hours and continued on alternate days.

(ii) *Lactose.*—It is probably not quite correct to include lactose among the drugs, but it is particularly valuable in cases where flatulence and intestinal fermentation are troublesome, and it may be used in place of sugar and glucose. In chronic constipation, it is useful as a mild laxative.

(iii) *Plantago ovata.*—It is known in the vernacular as 'ispaghula' or 'isabgul' and is a well-known and popular remedy in chronic dysentery, on account of its emollient and demulcent effect. The seeds are thoroughly cleaned free from sand and grit with which they are mixed. Two to four heaped dessertspoonfuls are mixed with a little sugar and shaken up in a cupful of water and the mixture is then swallowed. The drug has no bactericidal action and its effect appears to be entirely mechanical. The seeds after ingestion become uniformly mixed with the intestinal contents so that they are spread uniformly over the entire surface of the mucous membrane. The irritated or ulcerated areas of the intestinal mucosa are soothed by the demulcent action of the mucilage, which is not acted upon by the intestinal juices. It thus covers the surface of these ulcers protecting them from further irritation. The drug is tasteless and in chronic constipation it produces a laxative action similar to that of agar (Chopra, 1936).

(iv) *Kaolin.*—Kaolin has been used for its adsorptive effect on the bacteria and their toxins and for the production of formed stools where looseness of the bowel is a predominant symptom. In a severe case of ulcerative colitis the entire colon, as a result of chronic inflammation and destruction of the epithelium, has lost so much of its absorptive power that very large amounts of the drug would be required, endangering the removal of necessary vitamins by adsorption. It, therefore, seems probable that

the potential dangers offset the potential value of this medication (Emery, 1937).

(v) *Opiates.*—In spite of the introduction of numerous substitution products it is doubtful if the action of opium can ever be excelled by any other drug for the induction of sleep, control of diarrhoea and increased frequency of motions, and the relief of abdominal pain. Tincture of opium in five to ten minim doses is invaluable for prompt relief. Compound tincture of camphor, in one drachm doses, is also useful. It is important, however, to discontinue the drug as soon as the desired therapeutic effects have been obtained.

(vi) *Maintenance of water balance.*—In cases of diarrhoea and vomiting it is imperative to maintain an adequate water balance, and for this purpose, when necessary, solutions of glucose (25 c.cm. of 25 per cent solution) should be administered intravenously, and normal saline solution subcutaneously.

(vii) *Calcium and parathyroid.*—Prolonged administration of calcium lactate (5 grains) and parathyroid extract (1/20 grain) appears to be beneficial in a number of cases.

II. *Local and surgical treatment.*—Surgical measures may have to be undertaken for palliation of symptoms or treatment of complications.

(i) *Transfusion of blood.*—A high degree of anaemia is not infrequent in ulcerative colitis and is due to continuous loss of small quantities of blood in the faeces. In these cases a small transfusion (200 c.cm.) twice weekly for three or four weeks may be carried out with benefit. On rare occasions transfusion of blood may be necessary as a life-saving measure. With neo-haemoplastin (Parke, Davis and Co.) excellent results are generally obtained, but failures are not infrequent, whereas repeated transfusions of blood may be successful. In massive haemorrhage morphine is indispensable as in duodenal haemorrhage.

(ii) *Medicated enemata.*—Since the disease affects all the coats of the large gut, the use of medicated enemata may be rightly regarded as illogical. Stronger antiseptics cannot possibly reach the deep-seated diseased areas and, on the contrary, may aggravate the patient's condition by further devitalizing the superficial ulcers and lead to delay in healing. Nothing can supersede a normal saline enema in these cases. Local instillation of cod-liver oil has been found to be beneficial. It was first tried by us empirically, as we were impressed with its encouraging results in some intractable ulcers of the skin. At first half an ounce of cod-liver oil was injected at night slowly with a rubber catheter, but in the majority of cases it was promptly rejected. In about a week's time retention of the oil was found to be fairly satisfactory. A better method consists of giving a 40 per cent emulsion of cod-liver oil with gum acacia. The emulsion is instilled two to four times a day in doses of two to four ounces with a gradual increase up to eight ounces (Spiegel, 1937). Marked improvement

is not usually noticed before three months. A 60 per cent suppository of cod-liver oil may also be used. The vitamin treatment, when successful, produces a brilliant result.

(iii) *Operative procedures.*—The object of the usual operative procedures is to give rest to the diseased parts by diverting the fæces through an artificial anus.

(a) *Appendicostomy.*—Although this operation is still recommended by many for the purpose of lavage, the result, in our opinion, can only be described as unsatisfactory.

(b) *Cæcostomy.*—This operation was performed with much greater enthusiasm in the past with the laudable object of short-circuiting the faecal contents and for providing prolonged rest to the diseased colon. The results do not, however, justify this operation. When the colon is extensively diseased, after a prolonged period of rest it is converted into such a mass of fibrosis that functionally it becomes useless and the cæcostomy remains as a permanent token of futile surgical interference.

(c) *Left colostomy.*—This may have to be performed either as a life-saving measure in case of intestinal obstruction associated with rectal stricture or as a palliative measure for extensive fistulæ and pelvic cellulitis. Unfortunately this may remain a permanent artificial anus.

(d) *Ileostomy.*—In the past ileostomy was advocated as a temporizing measure instead of colostomy, but usually the patient succumbed soon after (Lardennois, 1936).

(e) *Short-circuiting operations.*—Theoretically anastomosis between the ileum and the lower colon has been advocated, with or without excision of the remaining part of the large intestine. This operation is not a practical proposition for the simple reason that the rectum and the sigmoid are the parts which suffer most. Besides, few patients would be able to survive the severity of such a major operation.

(f) *Surgery of complications.*—Of the complications most commonly complained of, fistula-in-ano, fissure, and so-called 'piles' need mention. The golden rule is not to interfere unless there is some definite indication.

*Results of operative treatment.*—The results of operative treatment have been uniformly unsatisfactory; moreover, the simplest surgical interference entails a high rate of mortality (25 to 40 per cent). Unfortunately, the formation of an artificial anus is indicated in the neglected cases complicated by stenosis of the rectum or the sigmoid colon, perineal cellulitis or multiple fistulæ. Of the rare complications which require operative treatment, may be mentioned intestinal obstruction and perforation which are, however, usually attended with a fatal result.

#### *Prognosis*

At best, the prognosis is, if anything, better than in the past. In about 50 per cent of cases definite improvement takes place but the treatment must be prolonged and laborious. It is yet too early to say if recurrence can be prevented.

In the more chronic cases, even if the ulcers are healed, proneness to diarrhœa and mucous discharge tends to persist owing to gross damage to an extensive area of the large intestine and consequent impairment of its physiological function of absorption of fluid. Some peristaltic disturbance persists also owing either to the mechanical cause of widespread fibrosis or impairment of the neuro-muscular mechanism.

#### *Summary*

This review of chronic ulcerative colitis is based on the clinical study of 120 cases with special reference to diagnosis, pathological findings, radiological analysis and treatment.

1. Chronic ulcerative colitis may be regarded as a disease of the large intestines during the second and third decades of life with characteristic clinical and pathological features but without any specific bacteriological infection.

2. It has not been possible to determine any single aetiological factor for ulcerative colitis. It is possible that many factors combine to produce devitalization of the mucous membrane of the large intestine leading to chronic ulceration.

3. Of the aetiological factors, avitaminosis, allergy, faulty body mechanics, emotional disturbances, streptococcal infection, and dysentery require special consideration.

4. In diagnosis, the sigmoidoscopic appearances are usually conclusive. In early cases, several stages may be described for convenience. In the *first stage*, the mucous membrane of the rectum and the sigmoid shows signs of hyperæmia and inflammation. In the *second stage*, the œdematous mucosa is studded with greyish-yellow granules representing minute necrotic foci. In the *third or active stage* there is the typical moth-eaten appearance owing to the breaking down of these granules. The *healing stage* presents multiple indolent ulcers and scars, while in the more chronic stage multiple vascular granular polyps are seldom absent. In another group of cases, large chronic ulcers are found, which show little sign of healing owing to super-vention of secondary infection.

5. At an early stage, when no ulcers are present, the microscopic picture consists of capillary dilatation, diapedesis, and hæmorrhage. The granular stage corresponds to minute necrotic foci under the mucous membrane with occlusion or thrombosis of the deeper vessels. Multiple small ulcers are next seen in the moth-eaten granular mucosa. Within the deeper tissues there are scattered necrotic areas containing hyaline-like material in various stages of fibrosis.

6. In the analysis of our cases we have not been able to point to any particular organism as the exciting cause. The bacterial examination of fæces showed an incidence of only 4 per cent for *E. histolytica* and 3 per cent for bacillary dysentery. The non-dysenteric character of chronic ulcerative colitis is therefore clearly indicated. *Streptococcus faecalis* was isolated in only 4 per cent of cases. We have included

*Ps. pyocyanea*, *Bact. morgani*, *B. carolinus* and *B. meta-alkaligenes* in this investigation, because they appear to be incriminatory. The analysis of scrapings of ulcers of the rectum and the sigmoid also point to the non-specific character of these ulcers. Culture of blood was found to be uniformly negative.

7. From a radiological survey of our cases in this series some abnormality of the duodenal cap was present in 37 per cent, a 5-hour residue in the stomach in 28 per cent and other gastric anomalies in 5 per cent. The gastric residue is due either to pylorospasm or to atony. There was only one case of duodenal ulcer, the remainder came under the heading of duodenitis. The appendix was visualized in 33 per cent but a residue was obtained in only 3 per cent. Abnormalities of the cæcum were present in 17 per cent. At an early stage of the disease spasticity of the gut was usual; the descending colon (35 per cent) and the ascending colon (31 per cent) were almost equally involved. Hypermotility was seen in 10 per cent and was associated with diarrhoea. The lower gut appears to be more liable to stenosis, while dilatation of the ascending colon was present in 18 per cent and of the descending colon in 5 per cent. A 48-hour residue was obtained in 28 per cent, representing chronic cases with ulceration and narrowing of the lumen.

8. The percentage ratio between males and females was found to be 72 : 28. The signs and symptoms in the early stage are not very definite, but when well marked, diarrhoea, precipitate motions, discharge of blood and mucus are prominent features. The periods of remission are very variable, but each succeeding attack becomes more acute than the last one and brings about severe prostration and loss of weight. Clinically, four types may be differentiated, *viz.*, (i) infective, (ii) allergic, (iii) associated with avitaminosis, and (iv) neurasthenic.

9. There is no specific for this condition and treatment is generally protracted. A somewhat onerous and careful dietetic regime has to be maintained. Rest in bed with postural treatment is always important for maintenance of strength, control of fever and diminution of tenesmus and frequency of motions. A low-residue diet is recommended, but it must be made up of adequate calories and it must contain the necessary vitamins. Ascorbic acid (vitamin C) has an excellent styptic effect in rectal hæmorrhage. Vitamin-B complex has a beneficial effect, but it is as yet difficult to indicate the rôle it plays. There is little doubt that allergy, when present, is due to a particular protein or some unknown amino-acid resulting from incomplete digestion. In this group of cases 'Torantil' (Bayer) is worthy of trial. Elimination of mental worries is an important factor in recovery. Vaccines and sera do not appear to have any definite effect. Of the drugs, lactose and *Plantago ovata* (isabgul) are useful. Buffered citrate therapy and kaolin have also

their advocates. In spite of the introduction of numerous substitution products, it is doubtful if the action of opium can ever be excelled by any other drug for the induction of sleep, control of diarrhoea, and relief of abdominal pain in a really severe case.

10. Surgical measures may have to be undertaken for palliation of symptoms and complications. Transfusion of blood may be required either for severe anæmia or as a life-saving measure. Medicated enemata do not appear to be useful because the disease affects all the coats of the large gut. Rectal instillation of cod-liver oil or emulsion has been found to be beneficial. The object of the usual operative procedures is to give rest to the diseased parts by diverting the fæces through an artificial anus. Operative measures, such as appendicostomy, ileostomy and short-circuiting operations, are now seldom resorted to. Of the complications most commonly complained of, fistula-in-ano, fissure and so-called 'piles' need mention. The golden rule is not to interfere in these cases unless there is a definite indication.

11. At best the prognosis is, if anything, better than before. In about 50 per cent of cases definite improvement takes place with clinical cure but the treatment must be prolonged and laborious. It is yet too early to say if recurrence can be prevented. In the more chronic cases, even if the ulcers are healed, proneness to diarrhoea and mucous discharge tends to persist, owing to gross damage to an extensive area of the large gut, with consequent impairment of its physiological function of absorption of fluid and peristalsis.

#### Acknowledgments

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## ABERRANT PANCREATIC TISSUE IN THE ALIMENTARY TRACT

By M. M. CRUICKSHANK

LIEUTENANT-COLONEL, I.M.S.

Madras

THOUGH the presence of pancreatic tissue in the alimentary tract is still considered an infrequent anomaly, yet over 350 cases have been reported in the literature, since Klob in 1859 reported the first case. Of the heterotopias found in the alimentary tract the accessory pancreas is the commonest.

The most common sites are the stomach and duodenum and the most frequent pre-operative diagnosis is either gastric or duodenal ulcer. This is what is to be expected, when one considers the development of the pancreas.

'It is probable that accessory pancreatic tissue is formed from lateral budding of the rudimentary pancreatic ducts as they penetrate the intestinal wall, the mass of pancreatic tissue thus formed being snared off and carried by the longitudinal growth of the intestine either upward or downward' (Warthin). That such irregular budding does occur is evidenced by the finding of such buds in close proximity to the duodenal papillæ, especially the lesser.

Similarly, the presence of pancreatic buds in the gall bladder is explained by the lengthening of the common bile duct, as the gall bladder developed.

On the other hand, acquired heterotopias do occur, in the same way as epithelial heterotopias of the alimentary tract arise during the healing process which follows a chronic inflammatory lesion, where ulceration and loss of tissue have occurred. As an example of this, one may cite

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those instances where the healing epithelium of the stomach takes on the morphological features of small gut.

The significance or importance of the presence of aberrant pancreatic tissue lies, of course, in the frequency with which it is mistaken for gastric conditions, more especially, if mistaken for neoplastic growths.

The pancreatic nodule in the gut may be the exciting cause of an intussusception; it may cause pyloric stenosis or acute intestinal obstruction; it may be the seat of an acute or chronic inflammation or of a carcinoma.

Pathologically two types are described, the aberrant pancreatic nodule and the annular pancreas.

The former is a much more common type and is the form which gives rise to difficulties in diagnosis and in many instances goes unrecognized until encountered during the course of some abdominal operation.

The rarer annular pancreas encircles the second portion of the duodenum and gives rise to constriction of that portion.

This form has definite clinical importance in that it may give rise to all the signs and symptoms of high intestinal obstruction. Whereas the nodular type is discovered usually at operation, the annular type, unfortunately, is usually a post-mortem finding.

The relation of carcinoid tumours of the appendix and small intestine to pancreatic rests has been a subject for much discussion. Some pathologists have stated that both adenomyomas and carcinoids arise in pancreatic rests and that carcinoids were pancreatic rests in which only the islet cells of Langerhans appeared. Masson and others have, however, shown that no such relationship exists and that carcinoids arise from chromaffin or argentaffin cells in the crypts of Lieberkühn. Moreover, carcinoids are found most frequently in the appendix, while pancreatic tissue has never apparently been found in the large bowel.

### Report of a case

A Hindu, male, aged 25 years, was admitted into hospital, complaining of pain in the upper region of the abdomen, which had lasted off and on for over two years.

*Family history.*—Nothing relevant.

*Previous illnesses.*—Nothing relevant.

*History of present illness.*—Has suffered from attacks of epigastric pain for two years. These attacks last anything from three to ten days and are followed by free intervals varying from four to eight weeks, but latterly the intervals have shortened to one week. The pain comes on about half an hour after taking food and lasts for about three to four weeks. The pain is relieved by vomiting which is spontaneous, but is on occasions induced. The vomit has occasionally been streaked with blood and the patient has, so he states, passed dark tarry-looking motions. Appetite has

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