Summary of Results

Category	Group A (Less than 1 Year)		Group B (1-2 Years)		Group C (Over 2 Years)		All Groups	
	No.	%	No.	%	No.	%	No.	%
Pain-free	13	29	11	26	2	20	26	27
Well controlled ..	11	25	20	48	8	80	39	41
Poorly	3	7	3	7	0	0	6	6
Failed	17	39	8	19	0	0	25	26
Total	44	100	42	100	10	100	96	100

Duration of Treatment.—The duration of treatment varied widely. On the one hand one patient took the drug for a fortnight and then remained pain-free for a year; on the other a patient took the drug continuously for two years, had a remission for four months, and then was started on carbamazepine again on return of the pain.

Failed Treatment.—A more detailed analysis of the results in the 25 patients (26%)—17 in group A and eight in group B—who were regarded as having failed to benefit is of interest. Four failed to respond despite adequate dosage, seven made a promising response initially but relapsed subsequently while on a higher dose of up to 1,400 mg. daily, and in 14 the drug was withdrawn because of side-effects. Of these 14 patients the drug was withdrawn in 10 because of a rash, in two because of severe giddiness, in one because of diarrhoea, and in one because of excessive drowsiness. It may be argued that withdrawal of the drug because of side-effects does not indicate that the drug had failed to control the pain. The converse was usually the case, but a therapeutic failure in the practical sense is implicit.

Age.—Four observations were noted in relation to age. Seventeen of the 96 patients were under the age of 50, but differed in no other respect from the remainder. The two patients who had the drug withdrawn because of severe giddiness and the one who stopped taking it because of marked drowsiness were all over 80 years of age. It is our impression that these particular side-effects increase in frequency and severity with increasing age. No similar trend was evident as regards the incidence of the rash.

Discussion

It is clear that a useful proportion of patients treated with carbamazepine can be maintained in reasonable comfort for periods up to two and a half years. There is no suggestion that the rate of relapse on adequate dosage of the drug increased with the duration of treatment; indeed, the converse is suggested. As may be expected group A, with a follow-up period of less than one year, showed the highest failure rate, but, even in this group, if the pain-free and well-controlled patients are combined then 54% did well on the drug. This is comparable with the result of a clinical trial of carbamazepine versus placebo over an eight-week period (Campbell, Graham, and Zilkha, 1966).

In group B, with a follow-up period of one to two years, 74% of the patients on the drug did well; and in group C, followed up for over two years, all 10 patients (100%) did well. Overall, and taking the three groups together, 68% of the patients receiving carbamazepine did well.

Of the 25 patients (26%) who were regarded as failures of treatment with carbamazepine, 16 eventually required operative measures. It is accepted that this proportion will vary according to the clinician's criteria of satisfactory control and the individual patient's reaction to pain.

Summary

The results of treating 96 patients suffering from trigeminal neuralgia with carbamazepine (Tegretol) are given. Of these patients 68% did well on the drug, and were kept comfortable for periods up to two and a half years.

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Idiopathic Ulcerative Colitis in the African: a Report of Four Cases

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Ulcerative colitis appears to be a rare condition in Africans. After many years of personal experience in Uganda, Trowell (1960) wrote: "There is no report in the literature of an African suffering from this disease and none has been encountered in the practice of (Mulago) Hospital. It is important that the first detected case should be carefully recorded, together with an assessment of incidence." The geographical distribution of ulcerative colitis was reviewed in a leading article in the *B.M.J.* (1962), and the difficulty of assessing the frequency of the disorder in the tropics was commented on. There were references to undoubted cases reported from Egypt, Brazil, Uruguay, Japan, and Israel, but not from tropical Africa.

Four African patients with ulcerative colitis were seen and diagnosed at Mulago Hospital during 1964; three were reported at a meeting at Kampala in June 1964 (*B.M.J.*, 1964) and a fourth was seen later in the year. The four patients are reported on in detail. It is believed that this is the first detailed account of ulcerative colitis developing in Africans in tropical Africa.

All four patients lived in Buganda and belonged to the Baganda tribe, which is the predominant tribe around Kampala and accounts for 43% of medical admissions to Mulago Hospital (Shaper and Shaper, 1958). Two were men and two women, and their ages were 30, 44, 51, and 58 years. Age at onset of the disease ranged from 29 to 52 years, and duration from one to 12 years. The diagnosis of idiopathic ulcerative colitis rested positively on typical sigmoidoscopic or radiological appearances in all of the patients and on beneficial response to corticosteroids alone in three of them, and

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negatively on the repeated failure to detect any pathogenic organisms in any of them or to influence favourably the course of the disease before steroids in three. One case, after an early fulminating episode, continued as the intermittent type. The other three were of the chronic continuous type, one showing a "segmental colitis" in the barium-enema examination. A study of the psycho-social background was made in each case.

Case 1

A businessman aged 30 years gave a history of one year's persistent diarrhoea with loose motions by day and night, the stools being watery, always containing mucus, and sometimes containing blood. His general health had not suffered. His stools had been examined frequently, but parasites or pathogens were never isolated. Several courses of a sulphonamide and one course of emetine had proved ineffective. Sigmoidoscopy provided the first major clue to the diagnosis when it revealed an inflamed, friable, finely granular mucosa covered by thick mucus. Histologically a biopsy fragment of the mucosa was infiltrated by neutrophils, eosinophils, and plasma cells. Barium enema demonstrated admirably the loss of haustral pattern, moderate luminal narrowing, and rigidity of the colon so characteristic of the advanced disease, together with incompetence of the ileocaecal valve and dilatation of the terminal ileum. He was placed on prednisone 45 mg. daily. Frequency of bowel action decreased, blood disappeared from the stool, and six weeks later the mucosa was normal on sigmoidoscopy. Prednisone was reduced and discontinued without a relapse ensuing, though mild diarrhoea persisted.

The patient was a Muslim and an ambitious businessman, having recently or currently undertaken several enterprises which involved him in considerable physical and mental strain. One had in fact brought him into conflict with the law. On top of this he had a complex home situation, all four of his wives being pregnant at the time his symptoms started. He was exceptionally co-operative, polite, and anxious to please. In hospital his bedside locker was always scrupulously clean and tidy. His shop, which was visited after his discharge from hospital, was also exceptionally neat and efficiently organized, and he was clearly keen to please his customers.

Case 2

The findings in Case 2, a man aged 44 years, were similar to those in Case 1, but the history was completely different in that he had had recurrent attacks of bloody diarrhoea over the past 12 years. Pain and swelling of both knee-joints accompanied the first attack but never recurred subsequently. The relapse which caused his hospital admission in 1954 was very severe and led to loss of weight, anaemia, and hypoproteinaemic oedema (serum albumin 1.3 g./100 ml.). He required blood transfusion. Without specific therapy he gradually improved. The diagnosis was not suspected then or during subsequent relapses until 1964, when sigmoidoscopy and barium enema revealed the typical changes. Rectal biopsy showed one suspicious area of what could be early carcinoma-in-situ. A subsequent biopsy has shown no change. His response to prednisone was excellent, though not complete.

After weaning at the normal age the patient was sent to the home of a foster mother (? relative), to whom he became deeply attached and whose death, while he was still a young boy, caused him deep grief and marked anxiety, as he had to stay in the house alone. His first wife bore him no children and left him in 1955 because of his illness and resulting poverty, and he then became dependent on his parents. In 1958 he married again, but remained childless. He was happy with his second wife, but was desperately anxious not to upset her in case she too left him. While financial worries were considerable he denied repeatedly that anxiety over them or other matters was actually associated with relapses. He seldom drank milk and rarely ate milk products. He was quiet and rather shy, anxious to please but not fussy, obsessional, or ambitious.

Case 3

Sister P. was a nun aged 51 years. She had had diarrhoea with mucus and intermittent blood for one year. The symptoms were

not severe. Sigmoidoscopy showed acutely inflamed friable mucosa without ulceration. Barium enema was normal. She responded strikingly to prednisone, the diarrhoea and rectal inflammation rapidly subsiding. Variable diarrhoea, never severe, recurred after prednisone was stopped, but mucus and blood were not seen again.

The patient had lived a completely secluded life in her convent since the age of 13 years, having virtually no contact with her family, her tribal life, or the country at large. She was confused by the outside world and its complexities. She was gentle, rather slow, and extremely anxious to please.

Case 4

A housewife aged 58 years had had variable left-sided abdominal pain and diarrhoea with blood, mucus, and even pus for six years. While sigmoidoscopy showed an almost normal mucosa apart from a tendency to bleed at 25 cm., barium enema revealed a segment of colon, extending from the splenic flexure to the rectum, which was smooth, narrow, and lacking in haustrations. As her symptoms were not severe, she was not given prednisone but was followed up in the out-patient department.

The patient lived the life of a cultivator without any obvious worry except past anxiety over the rearing of a large family. She drank milk, perhaps $\frac{1}{2}$ to 1 pint (284 to 568 ml.) daily. She appeared friendly and relaxed, and co-operated normally. She was not over-concerned about her disease.

Discussion

Why is ulcerative colitis not being seen in the African in tropical Africa? Following our initial report, Pillay in correspondence mentioned having seen four Africans with the disease in Durban (Pillay, 1964). No doubt other cases have been observed but have not as yet been reported. Even so, the more florid manifestations could scarcely be missed clinically, whereas milder chronic or intermittent types may be escaping detection because sigmoidoscopy, far less barium enema, cannot often be carried out in patients with obscure or persistent diarrhoea in most places in tropical Africa. A true assessment of incidence, then, is impossible at the present stage.

The aetiology of the disease remains uncertain. As it is rarest in lands where the hordes of intestinal pathogens are greatest, an infective cause seems more than ever unlikely. Even in the more highly developed countries themselves the disease is less common in those sections of the populace whose hygienic standards tend to be generally inferior—for example, in New Zealand it is relatively rarer in Maoris than in white people (Wigley and MacLaurin, 1962) and in negroes in the United States (Weiner and Lewis, 1960; Reinhart, 1961; Hijmans and Enzer, 1962). While these differences may also be explained on a genetic basis, it appears that among immigrants into the state of Israel there is a greater prevalence of ulcerative colitis in those from Europe and America than in those from Asia and Africa (Birnbau *et al.*, 1960). The inference is that there is a negative correlation between the prevalence of intestinal infections and ulcerative colitis.

The association of ulcerative colitis with bacillary dysentery has been discounted (Brown and Bagen, 1938); that with amoebic dysentery has been postulated in at least a few cases (Davis, 1949; Stewart, 1950). Amoebic dysentery is an uncommon cause of admission to Mulago Hospital; there were 20 cases of amoebiasis in the 1957 analysis of hospital admissions (Shaper and Shaper, 1958) and eight cases of parasitologically confirmed amoebic dysentery in 1964. It did not appear to be an aetiological factor in our series.

The beneficial effect of corticosteroids has greatly intensified interest in the hypothesis that ulcerative colitis is a "hypersensitivity" disease (Broberger and Perlmann, 1959, 1962; Klavins, 1963). Milk has been postulated as an external antigen (Truelove, 1961; Taylor *et al.*, 1964), and early weaning on to cow's milk as a predisposing factor (Acheson and Truelove, 1961). Among the Baganda, however, neither cow's milk nor

goat's milk is consumed by the majority (Rutishauser, 1963), whereas in certain other tribes in Uganda in which milk is consumed in large quantities no case of ulcerative colitis has yet been reported. Of the two patients in our series who were asked about consumption of milk and its products, the more severely affected took them only occasionally. The effects on our patients of withholding and then reintroducing milk and its products were not observed. The likelihood that any of our patients would have been reared on cow's milk in infancy is extremely remote, considering the local conditions then.

Finally there is the psychogenic hypothesis. The patient may have a susceptible temperament, being over-conscientious, over-dependent on the approval of others, subject to inner conflict, hostility, anxiety, rebelliousness, and guilt, and likely to have a history of psychosomatic or psychiatric illnesses; psychotherapy alone may benefit his ulcerative colitis (Paulley, 1950; Grace and Wolff, 1951; Fullerton *et al.*, 1962). An emotional crisis may itself precipitate the onset or a relapse (Brown, 1963). In our series Cases 1, 2, and 3 had at least some of the personality traits, and Case 1 (but not the others) admitted an association between mental stress and bowel symptoms.

No single hypothesis can claim to explain all cases of ulcerative colitis. The very severe forms of the disease seem to be genuinely rare in Africans, while the milder forms, if occurring, may be "buried" beneath the great mass of infective diarrhoeas and may thus remain undetected. The explanation could lie in the rarity of early weaning, high milk consumption, or the predisposing personality type. Among the sophisticated groups in African society, however, where a more European type of diet is taken, where attendance at a specialist centre for special investigations is easier, and where exposure to new mental strains is commoner it may be that this disease will turn out to be not so rare. It will not be the first of the so-called diseases of Western civilization where this has proved to be the case.

Summary

So far as can be ascertained, no detailed reports have previously been made of ulcerative colitis developing in an

African in tropical Africa. Four cases are recorded in whom the history and investigations were typical of this disorder. Three patients showed some of the personality traits said to be typical, and in one the onset of the disorder was related to psychological stress. Relevant psycho-social data are mentioned and the aetiology is discussed. Causes are suggested for the present apparent rarity of the disease in Africans in tropical Africa, where, however, it conforms to the world pattern of being relatively uncommon in less sophisticated communities. It is postulated that with increasing sophistication the disease may be seen more frequently in the future in tropical Africa.

Our thanks are due to our colleagues for allowing us access to their patients, and particularly to Dr. F. J. Bennett, reader in preventive medicine at Makerere Medical School, for interviewing all the patients in connexion with their psycho-social background. Dr. J. H. Roberts carried out the barium-enema examination and made the report on Case 4.

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Preliminary Communications

Dose of Anti-D Gamma-globulin in Prevention of Rh-haemolytic Disease of the Newborn

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Recent work by ourselves (Clarke and Sheppard, 1965; Woodrow *et al.*, 1965) and others (Preisler and Schneider, 1964; Freda *et al.*, 1965; *Medical World News*, 1965) has shown that Rh-negative women can be prevented from being immunized by their Rh-positive foetuses. The method used has been the intramuscular injection of 5 ml. of high-titre incomplete anti-D gamma-globulin given shortly after delivery. This eliminates any Rh-positive foetal cells which may have leaked across the placenta at delivery or before. Evidence for protection is the absence of immune antibodies six months after delivery among the treated women and their presence in a proportion of the control groups. So far, in all the clinical trials reported, 21 out of 94 untreated controls have produced immune antibodies, whereas none out of 78 treated with anti-D gamma-globulin has done so (*Medical World News*, 1965).^{*} It must be emphasized, however, that the effects of second

Rh-positive pregnancies in the group of treated mothers will have to be observed before one can be sure that protection is complete. If it is, the prophylactic treatment of women at risk will necessitate large supplies of gamma-globulin, which is expensive to make and will require many volunteers to produce. It is therefore, as pointed out by Gorman *et al.* (1965), very appropriate at the present time to find out the minimum dose of gamma-globulin which is effective, and this communication presents some evidence on the matter.

PRESENT EXPERIMENT

In a recent experiment we obtained 12 Rh-negative male volunteers and injected intravenously 5 ml. of Rh-positive ABO compatible foetal blood into six of them and 1 ml. into the remainder. Half an hour later two individuals in each of the two groups were given intramuscularly 0.5 ml., 1.5 ml., or 3 ml. respectively of our high-titre anti-D gamma-globulin (titre in albumin 1:2,560) prepared by Dr. W. d'A. Maycock

^{*} These overall figures were given in October 1965. We have no later data from all the centres, but in those using our criteria for the trial (Woodrow *et al.*, 1965) the results at present (January 1966) are that one out of 40 of those treated and 12 out of 42 controls have produced immune anti-D six months after delivery.