et al. (1961). In the present series it has been a serious problem—two patients being initially resistant and seven after a good initial response developing resistance and remaining so to increased doses. Thus resistance to the drug led to a failure of treatment in 9 (41%) of the 22 patients.

In a small personal series of 12 Indian and European hypertensive patients treated with guanethidine neither initial nor acquired resistance has been seen and dosage has been of the order of 25 to 75 mg. daily. Many of these patients have been satisfactorily controlled for many months.

That African patients from East Africa respond satisfactorily to ganglion-blocking drugs has been shown by Somers and Gitau (1959) with mecamlamine and by Somers (1961b) with pempidine. Experience in this hospital with mecamlamine, prior to using bretylium and guanethidine, was satisfactory.

Why this difference in response to treatment in these African patients occurs is obscure but is clearly a matter of great physiological and pharmacological interest. It has been suggested by Zaimis (1961) that acquired resistance to guanethidine is due to the sensitization of peripheral arterioles to the local effects of circulating catecholamines, and they warned against the use of excessive dosage. In this context it is of interest that in four of the resistant patients in the present series the diastolic pressure actually increased while dosage was being built up in an endeavour to gain control of the blood-pressure, and then fell when the drug was discontinued. Guanethidine is also known to cause increased noradrenaline release in animals. In man intravenous injection leads to an initial rise of blood-pressure without increase in the cardiac output. This is presumably due to muscle and visceral vasoconstriction (Dollery *et al.*, 1961).

The therapeutic efficiency of guanethidine may depend on the balance that is struck between its relaxant effect on peripheral blood-vessels from sympathetic-fibre blockade and the tendency towards sensitization of these vessels to circulating catecholamines, and possibly also to an increase in the amount of these amines. It may be that some dietary or metabolic factor in African subjects enhances, to a variable degree, these undesirable effects. It must be noted that unexpected increased sensitivity to guanethidine can occur, as is illustrated by the patient described above who after good control on large doses became very sensitive to the hypotensive effects of the drug and was then controlled on a very small dose.

The possible causes of this drug resistance can only be a matter for speculation at this stage. It is to be hoped that further studies will be made.

Summary

The use of guanethidine in a small series of African patients is described. Drug resistance as a serious problem has not previously been recorded, yet in this series it led to failure of treatment in 9 out of 22 (41%) patients. Two of these were initially resistant and seven developed resistance rapidly. Resistance to the drug has not been a problem in European and Indian hypertensives in Mombasa.

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TREATMENT OF PERFORATED DIVERTICULITIS COLI

BY

M. D. M. STAUNTON,* M.B., F.R.C.S.

Surgical Registrar, Morriston Hospital, Swansea

Perforated diverticulitis of the colon is not a common condition. Martin and Adsit (1945) estimated that it occurred in 2% of cases of diverticulitis. With the increase in life expectancy of the community there is no doubt that the incidence of diverticulitis coli will also increase, and result in a corresponding rise in the number of cases with complications.

The following account is based on 14 cases of acute perforated diverticulitis of the colon treated at Morriston Hospital in the four years 1955–9. During this period 72 other cases of diverticulitis were admitted to the same hospital; thus 16.3% of cases of diverticulitis treated as in-patients presented with perforation. Smithwick (1960) estimated an incidence of 13.4% in a total of 545 cases.

The relative incidence is best arrived at by comparing the incidence of perforated diverticulitis coli with that of acute appendicitis: during the period under study 1,402 cases of appendicitis were operated upon, giving a relative incidence of 1 case of perforated diverticulitis coli to every 100 cases of appendicitis. MacLaren (1957), in Edinburgh, found 26 cases of perforated diverticulitis among 2,322 cases of acute appendicitis. He classified cases of perforated diverticulitis into those that give rise to a faecal peritonitis and those that give rise to peritonitis of a purulent nature. These differences are dependent on the size of the perforation—a large perforation allows the escape of faeces into the peritoneal cavity, while a pinhole perforation usually results in a purulent peritonitis. Another factor in the causation of purulent peritonitis is that an abscess in a diverticulum may rupture into the peritoneal cavity but, owing to the fact that the neck connecting the sac to the lumen of the bowel is occluded by inflammation,

*Now at Royal Marsden Hospital, London.

no faeces can escape. The present series contained one case of faecal peritonitis and 13 cases of purulent peritonitis.

Clinical Picture

Six of the patients gave a history suggestive of previous attacks of diverticulitis.

Symptoms.—Pain is the first symptom, and is usually of a vague colicky nature situated in the lower abdomen, later followed by severe generalized abdominal pain. Six patients had a sudden onset of severe generalized pain. Symptoms were usually present 12–24 hours before admission, but in two cases they occurred three days and in one case five days before. Vomiting was present in half the cases and pyrexia was a constant finding.

Signs.—The general state depends on the degree of peritonitis: faecal peritonitis rapidly gives rise to a severe degree of shock, though many of the patients with purulent peritonitis were notable for their fit condition. The abdominal findings are those of peritonitis, and in most cases these are confined in the lower abdomen. An interesting point is that five patients had maximum tenderness in the right iliac fossa. The reason for this is that the apex of the sigmoid colon in those cases is situated to the right of the sacral promontory. Rectal tenderness was severe in only three cases. The sex-and-age distribution is shown in the Table. It comes as a surprise to find that most of the cases occurred in the decade 45–54. There is a preponderance of male over female cases.

Age and Sex Distribution in Series

Age:	35–44	45–54	55–64	65–74	Total
Males ..	1	5	3	1	10
Females ..	1	1	1	1	4

Treatment

Treatment.—Treatment was surgical in all cases. Patients with shock were first treated by fluid, plasma, and electrolyte replacement. All received systemic antibiotics, usually starting immediately after operation. A right paramedian incision was usually made, but if a right gridiron incision was first used it was closed when the diagnosis was ascertained and a right paramedian incision made.

Three different procedures were employed in the treatment of these cases.

1. Local Repair and Drainage

Four cases were treated in this manner. At laparotomy the site of perforation was identified then closed by interrupted catgut sutures and reinforced by an omental patch. Free pus was aspirated from the peritoneal cavity and the abdomen closed with a corrugated-rubber drain leading down to the perforation site. Two deaths occurred.

Case 1.—A man aged 49 with a perforated ascending colon died from pulmonary embolism on the fifth day after operation. At necropsy free pus was present in the peritoneal cavity.

Case 2.—A woman aged 67 with purulent peritonitis due to a perforated sigmoid colon died seven days after operation. Necropsy revealed widespread peritonitis, and further leakage had occurred at the site of perforation.

2. Local Repair with Proximal Colostomy

Five cases were so treated. The local repair was as described in group 1. The proximal colostomy was sited in the transverse colon in two cases and in the iliac colon in the remaining three. Two deaths occurred in this group.

Case 3.—A man aged 62 had a perforated sigmoid colon with purulent peritonitis. Proximal left iliac colostomy was performed and death took place five days later. At necropsy widespread peritonitis was present, due to a further leak at the site of repair.

Case 4.—A woman aged 64 was found at operation to have a large perforation in the sigmoid colon with widespread faecal peritonitis. Local repair with right transverse colostomy was performed. Death took place 24 hours later. At necropsy widespread peritonitis was found.

3. Exteriorization of Affected Loop

This was performed in five cases with no deaths. All were cases of purulent peritonitis with perforations in the sigmoid colon.

Method.—After identification of the perforation site the loop of sigmoid colon is mobilized. This is done by freeing the bowel from adherent structures. A very common finding is an inflammatory band tethering the apex of the sigmoid colon to the posterior abdominal wall, usually to the right of the sacral promontory. When this is divided it is surprising to see how much mobility the sigmoid loop so gains, and subsequently it is possible in most cases to exteriorize the affected loop via a Rutherford Morison type incision in the left iliac fossa.

Mortality

There were four deaths among the 14 patients in this series. Graham (1937) reported 4 deaths among 11 patients and Eggers (1941) 8 out of 12. MacLaren showed that during the period 1935–55 there were 33 deaths among 75 cases of perforated diverticulitis, but in cases of faecal peritonitis death occurred in 15 out of 20. The definitive treatment of the diverticular lesion is outside the scope of this paper.

Discussion

All argument centres in the treatment of these cases. Local repair of the perforation with drainage is not a reliable method, as shown by the mortality in this series. The local repair is never convincing owing to the fatty and oedematous nature of the bowel at the site of perforation; the wonder is that it ever succeeds, not that it fails so often.

The main objective in the treatment as enunciated by Crile (1954) is the elimination of the source of contamination. Exteriorization of the affected loop of bowel always achieves this. Diversion of the faecal stream by proximal colostomy is an indirect method of attaining this objective, but it is uncertain in its effect and often fails.

Exteriorization has been advised by many surgeons, including de Courcy Wheeler (1930), Black (1931), Bacon (1948), and Aylett (1954); but the majority of surgeons, while admitting its theoretical advantages, felt that, owing to the surrounding adhesions and the fatty oedematous state of the bowel, it would be possible to use it in very few cases. On reviewing the 14 cases reported here I feel that it would have been possible to perform exteriorization in 12 of them:

therefore it is fair to say that the majority of sigmoid perforations could be treated by exteriorization.

Most surgeons, including Wells (1949), Sedgwick (1951), Patton (1953), and Patterson (1955), favour local repair, with proximal colostomy. This is technically easy, but it must have a higher mortality because in some cases further leakage will occur from the site of perforation despite the proximal colostomy, as shown in Case 3 above. Also, the nearer the colostomy is to the perforation the more effective it should be—for instance, a left iliac colostomy for a sigmoid perforation.

Ryan (1958) treated four cases by immediate resection and end-to-end anastomosis to reconstruct the colonic tract. The results were excellent—all four patients made an interrupted recovery. It is very doubtful, however, whether if resection and anastomosis were widely used in the treatment of perforated diverticulitis there would be any overall reduction in the mortality, because to the definite mortality of emergency colonic anastomosis would be added the deaths from the severity of the primary perforation. The simple and safe method of exteriorization is therefore to be preferred. In the few cases where exteriorization is not possible the wisest course would be to perform resection of the affected area of sigmoid colon by the Hartmann method.

Summary

Fourteen cases of perforated diverticulitis are recorded. The relative incidence is assessed and the composition of series noted. The treatment was always surgical, and the benefits of exteriorization of the lesion over either local repair or local repair and proximal colostomy are shown by the fact that all five patients treated by exteriorization survived while among the nine treated either by local repair alone or with a proximal colostomy there were four deaths.

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The two addresses given at the afternoon session of a conference held by the British Council for the Welfare of Spastics in December, 1960—"Education for Life After School," by Mr. H. B. DAVIES, B.Sc. (headmaster, Thomas Delarue School, Tunbridge), and "From School to Work," by Mr. M. O. DAVIES, B.A. (senior youth employment officer, London County Council)—have been published by the Council in a leaflet called *Spastic School Leavers: Employment?* (Price 1s. 6d., post free, from the B.C.W.S., 13 Suffolk Street, Haymarket, London S.W.1.)

TWO CASES OF CHLOROQUINE-INDUCED RETINAL DAMAGE

BY

J. N. ORMROD, M.B., F.R.C.S.

Consultant Ophthalmic Surgeon, Kent County Ophthalmic and Aural Hospital, Maidstone

Chloroquine and allied substances are being used to a considerable extent in the treatment of rheumatoid arthritis and various skin diseases. Corneal changes resulting from the systemic use of chloroquine are now a well-recognized entity, and there are numerous reports in the literature of this not infrequent side-effect of chloroquine medication.

Retinal changes from chloroquine are fortunately much less frequent, but are nevertheless very important because they lead to irreversible changes with serious visual impairment, for which, as yet, there is no effective treatment.

So far there are only a few reported cases in the literature, and it would thus seem advisable to report the following two new cases which I have seen during the past 18 months.

Case 1

A man aged 28 was first seen in 1955 in the skin department of a local hospital complaining of a rash on the face and forearms of three years' duration; he also gave a history of a blistering eruption of the ears, especially severe when exposed to sunlight and heat. A diagnosis of "light sensitivity" was made and treatment was begun with tablets of chloroquine 150 mg. twice daily, together with a local application of a light-screening agent. Later medication was changed to "avlochlor" (chloroquine phosphate) 250 mg. twice daily, and he remained on this until shortly before December, 1959, when he was seen again in the skin department complaining of difficulty with night vision, and some difficulty in seeing steps. A refraction carried out four months previously had shown an unaided vision of 6/5 in each eye. He was referred to me in March, 1960, by the skin consultant, who drew my attention to an article reporting similar eye symptoms following chloroquine therapy (Hobbs *et al.*, 1959).

On examination I found him to have an unaided vision of 6/9 in each eye. There were subepithelial changes in the cornea with some oedema, the appearance of the cornea of each eye being consistent with chloroquine medication. The maculae showed pigmentation and there was attenuation of the retinal arteries. Visual-field examination showed a dense absolute ring scotoma sparing the macula and extending into each upper temporal field (Fig. 1). In view of the symmetrical nature of the field defects a full neurological examination, including lumbar puncture, was carried out, but with negative results. He has been seen at intervals and, although he has had no chloroquine or similar drug since November, 1959, the fundus appearance and visual fields have remained unchanged. He has been forced to change from his original job of milk roundsman, since it was felt that it was no longer safe for him to drive a vehicle.

Case 2

A man aged 53 was first seen by me in August, 1961, when he was referred by his general practitioner, who reported that his optician had noticed a fall in his corrected visual acuity from 6/6 to 6/18 in each eye over a period of nine months.