prednisone and prednisolone therapy. In all three cases radiological evidence of healing followed the institution of routine ulcer treatment, without the need for discontinuing the drug. In contrast, in two patients treated by Hart *et al.* (1955) dyspepsia improved when prednisone was substituted for cortisone.

The case recorded here is a further example of symptomless duodenal ulcer developing during prednisone therapy. Although the patient experienced some abdominal pain during the seven days before his death, this was not localized and was never severe, and at no time were either the symptoms or the clinical findings suggestive of perforation. In the absence of symptoms and of radiological evidence it is not possible to state accurately the date of onset of the ulcer, but the histological appearances leave no doubt that its duration was substantially less than that of the prednisone therapy.

There have been several reports of massive haematemesis (Pechet, cited by Bollet *et al.*, 1955; Bickel, 1955) and of intestinal haemorrhage (Muller, 1955) occurring during prednisone therapy. Pickert (1956) recorded a case similar to ours in which perforation of a symptomless duodenal ulcer, histologically acute, was the cause of death. Fentress *et al.* (1956) and Hess and Macpherson (1957) described cases of perforation, which were not symptomless, complicating treatment with prednisone and prednisolone respectively.

It is clear that symptomless perforation must be added to symptomless ulceration as one of the possible complications of prednisone therapy.

It would seem advisable to carry out frequent examinations of the stools for occult blood, as well as repeated barium-meal examinations where possible, during prednisone therapy. Antacids probably have some prophylactic value. Estimation of plasma and urine pepsinogen levels (Hirschowitz, 1955; Hirschowitz *et al.*, 1956) might become a practicable method for detecting the onset of peptic ulceration. The occurrence of epigastric pain, however mild, should be regarded as a danger signal.

Summary

A case of fatal perforation of a duodenal ulcer following two months' prednisone therapy for multiple myeloma is recorded. The ulcer was histologically of acute type, and was probably of two to four weeks' duration. It was virtually symptomless, and the subsequent perforation and peritonitis were attended by a minimum of symptoms and a total absence of physical signs.

We wish to thank Dr. J. S. Parkinson for permission to publish this case.

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The British Epilepsy Association gave a preview of its film "People Apart" at the Royal College of Surgeons this month. The film tells the public "the facts" about epilepsy. It was made by Guy Brenton, who won an "Oscar" for the best documentary film of 1955. The main actors are epileptics; there are no professionals. "People Apart" (35 mm. or 16 mm., 35 minutes, with sound) may be hired by private associations from the British Epilepsy Association, 136, George Street, London, W.1. (Hiring fee £2.)

Medical Memoranda

Intussusception and Acute Appendicitis

The association of acute intussusception with acute appendicitis in infancy and childhood is not a common one. The age incidence of the two conditions differs, intussusception being uncommon over 2 years and acute appendicitis uncommon under 2. In a small personal series of 12 consecutive operations for acute intussusception during the past year, only one infant was aged over 2 years; in a series of 75 operations for acute appendicitis during the same period, only one child was under 2.

Thompson (1955) records a case of caeco-colic intussusception complicating perforated appendicitis in an infant of 20 months, and gives reasons why the intussusception probably followed the appendicitis. He refers to a similar case of Lipin and Miller (1948): a man of 21 in whom acute appendicitis was complicated by intussusception.

The reverse sequence—acute appendicitis following intussusception—seems particularly uncommon. The following case is thought of sufficient interest to be recorded.

CASE REPORT

A healthy girl of 5 was admitted to hospital as an emergency case on March 13, 1955. The history was of attacks of colicky central abdominal pain and vomiting for the previous 36 hours. There had been no rectal bleeding. Examination showed her general condition to be satisfactory: she was neither shocked nor pyrexial. There was no tenderness or any other physical signs on abdominal examination.

She was kept under observation. Twelve hours later she developed another attack of severe abdominal colic and vomiting. Abdominal examination then revealed some central distension and a palpable mass in the right lumbar area. During this period her highest temperature was 99° F. (37.2° C.). The urine contained no pus cells on microscopy. A white cell count showed 28,000 per c.mm. (80% polymorphs). It was decided to operate. A diagnosis of intussusception was considered, but the leucocytosis was not explained.

A right paramedian incision was made and an intussusception found with its apex half-way up the ascending colon. This was reduced without difficulty and the gut was perfectly viable. The appendix appeared very slightly swollen, but did not seem acutely inflamed. In view of the leucocytosis, appendicectomy was performed. After completion of the operation the appendix was opened and found to contain frank pus. Mucosal ulceration was present, and it was felt that perforation would soon have followed. Histological examination confirmed the acute inflammatory process. The patient made an uninterrupted recovery without antibiotics, and was discharged on the twelfth post-operative day.

It is thought likely that the first event occurring here was the intussusception. The acute appendicitis probably followed when the base of the appendix was drawn up by the intussusceptum, precipitated by the appendix becoming obstructed by the neck of the intussusciptens. The following features confirm this view: (1) the absence of pyrexia and abdominal tenderness, due to the inflamed appendix being buried in the intussusception; (2) the first physical signs noted were those of abdominal distension and a mass; and (3) the intussusception was of the common ileo-caecal type starting just proximal to the ileo-caecal valve.

COMMENT

After reduction of an intussusception the appendix is often seen to remain blue and even show incipient gangrene after the gut wall has returned to normal. For this reason,

in the series of 12 intussusceptions referred to above, appendicectomy was performed in five cases, with no deleterious effects on post-operative recovery. No reference has been found to intussusception precipitating acute appendicitis by obstructing the lumen of the appendix. In view of the outwardly innocuous appearance of the appendix in the case described, it is felt justified to urge appendicectomy in intussusception if the appendix shows the slightest abnormality. This should apply especially to children over the age of 2. Gross (1953) states that "mere engorgement and swelling of an appendix is not a sufficient indication for appendicectomy. . . . The cautious operator will not remove the appendix unless it is gangrenous and its vessels thrombosed." A plea is entered to modify this attitude.

I should like to thank Mr. A. Gourevitch for permission to publish this case.

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Fatal Agranulocytosis During Treatment with Amodiaquine

Amongst the drugs more recently introduced both chloroquine and amodiaquine ("camoquin") have established a good reputation for safety in the treatment of malaria. In this disease, however, they are usually given in short courses. The extension of their use over long periods to treat chronic diseases such as lupus erythematosus and other skin diseases in which photosensitivity is an important factor introduces new hazards.

In the treatment of malaria, side-effects which have been reported include mild and transient headache, visual disturbances, gastro-intestinal upsets, and pruritus. After prolonged medication for suppressive purposes dermatitis, bleaching of the hair, and diminution of T waves in some or all leads of the E.C.G. have been reported (Goodman and Gilman, 1955). Side-effects are reversible on withdrawal of the drugs and only rarely become serious enough to contraindicate their use in this disorder.

In a recent review of the treatment with these drugs in lupus erythematosus (Dubois, 1956) two more potentially serious side-effects have been recorded—namely, thrombocytopenia and severe leucopenia—the former being encountered once and the latter three times in treating a series of 42 patients with chloroquine. In this series neither of these effects was encountered in treating 31 patients with amodiaquine. However, as these drugs are so closely allied chemically the following case of fatal agranulocytosis following treatment with amodiaquine seems worth reporting.

CASE HISTORY

A married woman aged 53 was admitted to hospital on September 26, 1956. Ten days previously she developed a sore throat and was presumed to have a quinsy. Three months earlier she had a rash on her face and forehead which appeared to be made worse by exposure to sunlight, and for this reason she was given amodiaquine. In all she received one tablet (200 mg.) of amodiaquine daily for nearly eight weeks, from July 24 to September 16. With the onset of the sore throat on September 16 the amodiaquine was stopped and "distaquine penicillin," 300,000 units, was given systemically daily for three days and subsequently by mouth. The temperature, which was initially 102° F. (38.9° C.), never responded to treatment, and just before admission she became irrational, was unable to open her mouth, and was thought to have some neck rigidity. The presence of meningitis was suspected.

On admission she was obviously very ill, jaundiced, and toxæmic. Temperature was 99.8° F. (37.7° C.). With much difficulty the mouth was opened and a sloughing ulcer surrounded by a zone of erythema was detected on the right tonsil. The left tonsil was also inflamed. There was marked fetor of the breath. Neither the cervical lymph nodes nor the spleen were palpably enlarged. The other systems shared no significant abnormality.

Investigations.—September 26: Hb, 90% (13.3 g./100 ml.); C.I., 0.95; red count, 4,760,000 per c.mm.; white cells, 3,500 per c.mm. (lymphocytes 100%); E.S.R., 48 mm.; P.C.V., 40%; M.C.H. 28 µg.; M.C.V. 84 cubic microns; M.C.H.C., 33.2%. September 27: Direct bilirubin, 1.2 g./100 ml.; indirect bilirubin, 1 g./100 ml.; total bilirubin, 2.2 g./100 ml.; alkaline phosphatase, 22.3 K.A. units; thymol turbidity, 1 unit; zinc sulphate turbidity, 1.5 units; total protein, 5.15 g./100 ml. (albumin 3.6 g., globulin 1.55 g.); albumin: globulin ratio 2.38:1. Widal reaction negative in all dilutions of patient's serum against the following: *Salmonella paratyphi B* O and H, *Salmonella typhi* O and H, *Brucella abortus*, *Brucella melitensis*, and non-specific *Salmonella* H. Urine: reaction acid; albumin trace; sugar nil. Microscopical examination—light deposit of amorphous urates only. No growth on culture. A negative test for quinine derivatives. White count 600 per c.mm. September 28: Sternal marrow showed a very marked hypoplasia of the granular series; the red blood cells showed some anisocytosis and polychromasia; erythropoiesis did not appear to be much affected; myeloid-erythroid ratio 1:4. Right tonsil: culture—large number of Gram-positive cocci seen. Left tonsil: culture—several epithelial cells and a number of Vincent's organisms present. A few colonies of *Staph. albus* and *Str. viridans* were grown. White cells, 450 per c.mm. (lymphocytes 99%, large monos. 1%). September 29: Paul-Bunnell, unabsorbed weak positive at 1:20, absorbed weak positive at 1:10. White cells, 350 per c.mm.

The patient was given one million units of soluble penicillin six-hourly from the time of admission, and in addition tab. prednisone, 10 mg. four times a day. The following day she was also given pyridoxine, 200 mg. daily. This was later changed to 50 mg. twice daily intravenously and 100 mg. daily orally. The patient failed to respond to therapy; the temperature remained elevated and the white count low throughout. She went steadily downhill and eventually died on September 30 at 6.50 a.m.

Post-mortem Findings.—At necropsy the outstanding abnormal findings were as follows. The brain showed some congestion and much oedema, but the central nervous system was otherwise normal. The fauces and tonsils were ulcerated and there was slight erosion of the lower end of the oesophagus. The large bowel as far as the splenic flexure was thickened owing to oedema. The lungs were congested. Small haemorrhagic areas resembling infarcts were visible. Both lower lobes were dark and oedematous, but there was no pneumonic consolidation. The pericardial sac contained 1½ oz. (45 ml.) of clear icteric fluid. The heart was dilated and the cut surface of the myocardium revealed diffuse fine fibrosis. The kidneys were of normal size, but early arteriosclerotic changes were visible. The liver was enlarged and had a nutmeg appearance. The spleen was about double normal size. The lymph nodes in the porta hepatis and mesentery were enlarged. The bone marrow appeared normal.

I am grateful to Dr. F. Macdonald, of Parke, Davis and Co. Ltd., for drawing my attention to the relevant literature, and to my colleague, Dr. R. A. Garson, who carried out the special investigations.

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