shortened by an average of two to three hours by the use of bemegride. We have gained support for these observations in another series of 20 patients without control observation and in a further 25 patients who were not so closely observed.

The dosage used in the present series was standardized for purposes of comparison, and in the great majority this proved to be satisfactory. In practice, it should suffice to give one dose and follow it with a second only if the patient is still drowsy (and not nauseated) half an hour later. Only very occasional patients have shown slight agitation or nausea after the first dose of 150 mg. and only 5 out of 55 have shown these toxic effects after the two doses used. As nausea or vomiting is likely to be one of the earliest toxic effects, there is advantage in giving the drug orally. There was no evidence that thyrotoxicosis or myxoedema predisposed to toxic reactions.

On the basis of the above findings, we can now recommend oral bemegride as a practical and safe means of shortening the period of drowsiness which follows barbiturate sedation. One oral dose of 150 mg. in 0.5% solution should be given, and be followed by a second in 30 minutes only if the patient is then still drowsy and not nauseated. In this series barbiturates had been given in order to carry out sleeping B.M.R. estimations. There are many other diagnostic and therapeutic techniques, however, which require sedation and have therefore usually necessitated admission to hospital. If such barbiturate sedation is terminated by bemegride these procedures can be simplified, and may then even be performed in the out-patients department.

Summary

A series of 13 patients sedated with barbiturates for the purpose of B.M.R. determinations were studied to evaluate the action of a barbiturate antagonist, bemegride. A two- to three-hour shortening of the drowsy period was noted after bemegride compared with a placebo.

Bemegride was given in two oral doses of 150 mg. in 0.5% solution at an interval of half an hour. Toxic reactions were few and related mainly to the second dose.

Bemegride appears to have considerable value in facilitating the performance of therapeutic and diagnostic procedures which need barbiturate sedation.

We thank the nursing staff of Hammersmith Hospital who co-operated in this trial; also Dr. Edmund Alcock, medical officer, A. & G. Nicholas Ltd., for generous supplies of megimide.

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The British Council for the Welfare of Spastics has published a pamphlet containing four addresses on cerebral palsy. They were given at a conference for doctors in Birmingham last October, under Professor J. M. SMELLIE'S chairmanship. Professor R. S. ILLINGWORTH discusses the "Early Diagnosis of Cerebral Palsy"; Dr. FRANCES BRAID "The Aetiology of Cerebral Palsy"; Dr. H. M. COHEN "Cerebral Palsy and the School Health Service"; and Mr. A. INNES, F.R.C.S., "The Management of Cerebral Palsy." The pamphlet (pp. 40) may be obtained from the council at 13, Suffolk Street, Haymarket, London, S.W.1, price 3s. 6d. (post free).

FATAL DUODENAL PERFORATION DURING PREDNISONE THERAPY

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Prednisone, or Δ^4 -dehydrocortisone, is regarded as superior to cortisone both because of its greater potency and because, within the normal range of therapeutic doses, it has less sodium-retaining effect with little tendency to produce oedema. Bollet *et al.* (1955), however, reported the development of symptomless duodenal ulcers, identified radiologically, in 3 of 18 patients receiving prednisone or prednisolone (Δ^4 -dehydro-hydrocortisone) for rheumatoid arthritis.

The following report concerns the development during prednisone therapy of a symptomless duodenal ulcer which remained unsuspected until perforation and peritonitis were revealed at necropsy.

Case Report

A man aged 61 was first admitted to hospital on April 20, 1956, complaining of bilateral rib pain and a purpuric rash. On May 5 a diagnosis of multiple myeloma was made by sternal marrow examination, and was confirmed biochemically and radiologically. There was no history of digestive upset. Treatment was with urethane for 25 days and cortisone for 8 days. On June 14 prednisone, 5 mg. three times a day, was substituted for cortisone, while urethane therapy was continued. He was discharged from hospital somewhat improved five weeks later, and continued to receive these drugs at home. On August 14 he was readmitted complaining of vague abdominal pain, constipation, and dyspnoea, of one week's duration. By this time he had received a total of 920 mg. of prednisone. He was pale, with a recurrence of the purpuric rash which had been observed intermittently for the past year, and there was evidence of considerable weight loss since his last admission. The abdomen was soft and was not distended. Tenderness was not elicited in any area, nor was there any guarding or rigidity. Bowel sounds were heard. The rectum was full of soft faeces, but there was no tenderness. Pulse rate 80 per minute; blood pressure 95/50 mm. Hg. He became comatose shortly after admission, and died four hours later.

Post-mortem examination showed that death had been due to generalized peritonitis following perforation of a duodenal ulcer. The peritonitis was maximal in the upper abdomen and right iliac fossa, and there was a frankly purulent exudate between liver and diaphragm. The ulcer, which measured 3 by 0.6 cm., was situated vertically on the posterior wall of the duodenum, immediately beyond the pyloric sphincter. Histologically, it was a peptic ulcer of acute type which, except at the site of perforation, was almost confined to the mucosa and submucosa, with a minimal degree of fibrosis and virtually no involvement of the muscle coat. The probable duration of the ulcer was two to four weeks. The remaining positive findings were those of multiple myeloma.

Discussion

While there have been reports of dyspepsia developing during prednisone or prednisolone therapy (Bunim *et al.*, 1955; Margolis *et al.*, 1955; Fisher, 1956), a more striking finding was that of Bollet *et al.* (1955), who observed radiological evidence of duodenal ulceration, without corresponding symptoms, in three previously ulcer-free patients on

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,