inflamed than the mucosa, and the cell reaction was largely polymorphonuclear. The outer surface showed peritonitis of apparently some days' duration. An occasional Gram-positive coccus was seen. Special staining revealed amyloid deposits in small vessels and in the basement membrane.

Discussion

The diagnosis of peritonitis was based on the sudden onset of upper abdominal pain radiating to the right iliac fossa and acute abdominal tenderness, followed later by rigidity and absence of bowel sounds. In retrospect, the episode three days previously was one of perforation with local peritonitis, and this was supported by histological examination. Before operation the gall-bladder was not suspected as the seat of disease, and it is probable that a reflex pylorospasm was responsible for the symptom-complex.

The significance of the relationship of onset of dyspepsia to the starting of treatment with prednisone is difficult to assess. It is known that peptic ulceration occurs more frequently with prednisone than with cortisone, but cholecystitis has not yet been described as a complication of either of these drugs. Because of deterioration in the general condition associated with persistent vomiting, prednisone was replaced by intramuscular cortisone. The stress associated with surgical trauma was covered by intravenous hydrocortisone.

Corticotrophin has been found to bring the temperature and pulse rate to normal levels within 12–36 hours after its administration (Beck *et al.*, 1950). It also causes a decrease of the leucocytes during the first few hours, with lymphopenia and eosinopenia. In the reported cases of patients undergoing treatment with corticotrophin and cortisone we found that the physical signs of all underlying diseases were obscured and there was a delay in diagnosis due to the reduction of inflammatory response caused by these drugs.

When an operation is contemplated on a patient undergoing treatment with corticotrophin and cortisone, care must be taken to ensure that large doses of cortisone are given immediately before and after the operation, because there is a possibility that, without taking this precaution, the patient may develop post-operative adrenal cortical insufficiency due to stress (Salassa *et al.*, 1953). As cortisone was withdrawn, adrenal stimulation with intramuscular corticotrophin was maintained. Adequate dosage of corticosteroids must be ensured, otherwise clinical features of adrenal cortical insufficiency develop quickly, the most important being restlessness, nausea, vomiting, weakness, hypotension, and coma. In treating the adrenal cortical deficiency state, intravenous hydrocortisone—the quickest therapeutic agent—gives an almost immediate response; oral cortisone acts in four to six hours, and intramuscular cortisone more slowly.

Because the severity of the post-operative renal failure was more marked than could be accounted for by the transient oliguria, the possibility of amyloidosis was considered and a special staining technique confirmed this in the specimen removed. Two months later the congo-red retention test (Unger *et al.*, 1948) was shown to be positive, 90% of the dye being retained after one hour.

In life the overall incidence of amyloid in rheumatoid arthritis is 4% (Fearnley and Lackner, 1955) and should be suspected in any patient with persistent and prolonged activity of the arthritis who has proteinuria, hepatomegaly, or splenomegaly.

Summary

A case of perforation of the gall-bladder in a patient with rheumatoid arthritis treated with prednisone is described. Histological examination of the gall-bladder revealed amyloidosis. The clinical features of the illness and its management are discussed.

We are grateful to Professor C. V. Harrison for the pathological report; to Mr. R. Shackman and Dr. E. G. L. Bywaters for their permission to publish this case; and to Dr. B. M. Ansell for her assistance.

REFERENCES

- Beck, J. C., Browne, J. S. L., Johnson, L. G., Kennedy, E. J., and MacKenzie, D. W. (1950). *Canad. med. Ass. J.*, **62**, 423.
Fearnley, G. R., and Lackner, R. (1955). *British Medical Journal*, **1**, 1129.
Salassa, R. M., Bennett, W. A., Keating, F. R., and Sprague, R. G. (1953). *J. Amer. med. Ass.*, **152**, 1509.
Unger, P. N., Zuckerbrod, M., Beck, G. J., and Steele, J. M. (1948). *J. clin. Invest.*, **27**, 111.

Medical Memoranda

Treatment of Acute Primidone Poisoning with Bemegride and Amiphenazole

Since its introduction as an anticonvulsant in 1950 primidone ("mysoline") has shown itself to be a valuable drug, particularly in grand mal. For this reason it has come to be used extensively; but, in spite of this, only one fatal case of acute poisoning with the drug has been reported—no doubt, among other things, owing to its relatively low toxicity. Up to the present it appears that only four cases of serious acute poisoning with the drug have been reported. Three of these cases were suicide attempts by adults, and one was a 4½-year-old child, in whom the poisoning was due to lack of supervision. Among the three cases of attempted suicide the amount of primidone taken by the first reported case (Arnold and Ceranke-Höfermayer, 1953) was 30 g. (120 tablets). This produced unconsciousness for 12 hours, followed by sleepiness for another two days. In another case, reported by Sciarra *et al.* (1954), a dose of 6.5 g. (25 tablets) only produced a deep sleep lasting four to five hours. In the third case, which was quoted by Morley and Wynne (1957), a dose of about 20–30 g. (80–120 tablets) led to death in the course of 12 to 24 hours. In the fourth case, reported by Morley and Wynne (1957), a 4½-year-old boy had taken about 12.5 g. (50 tablets), which caused loss of consciousness lasting about 36 hours.

In the case described below, a 57-year-old man had taken about 25 g. (100 tablets) of primidone in an attempt at suicide; this put him into a state of drowsiness, which passed into unconsciousness after about 36 hours. This lasted about 12 hours, after which unconsciousness was terminated by means of treatment with bemegride ("megimide," "malysol") and amiphenazole ("daptazole," "fenamizol"), which was obviously effective. About 40 minutes after the beginning of treatment the patient was quite lucid.

We have been unable to find in the literature a single case of primidone poisoning treated with these drugs. But, since they have a good antidotal effect against barbiturates, these drugs should obviously be tried. This is because primidone and phenobarbitone are closely related in chemical constitution, although they differ substantially in toxicity. Primidone can be regarded as a reduction product of phenobarbitone, one oxygen atom in the pyrimidine ring of the molecule being replaced by two hydrogen atoms linked to the same carbon atom.

CASE REPORT

A 57-year-old man with symptomatic epilepsy of some years' standing had for the past six months been put on primidone in a dosage of 2–3 tablets a day. His attacks had been controlled by that treatment. Earlier he had been suffering from mental depression, and had attempted suicide in August, 1956. For some time before admission he had again been depressed and had uttered threats of suicide. According to his own statement, in the evening of November 19 he took 100 0.25-g. primidone tablets with intent to kill himself. He was admitted to hospital on the following day, and brought with him an empty jar which had contained 100 primidone tablets dated November 19, 1956. He was admitted in a dazed condition, with slurred speech. He confirmed that he had attempted suicide with primidone.

On the morning of November 21 he was unconscious, but not very deeply, since pharyngeal reflexes were still present.

Blood values on November 21 were: Hb, 77%; R.B.C. 4,000,000; W.B.C., 6,900; residual nitrogen, 39 mg. per 100 ml. Unconsciousness continued throughout the day. As the patient soon became more deeply unconscious bemegride and amiphenazole were given in the evening on the same principle as for barbiturate poisoning. Isotonic glucose was given by intravenous drip. At 19.53 hours 50 mg. of bemegride and 15 mg. of amiphenazole were introduced into the intravenous drip. This was repeated at 19.56, 19.59, 20.04, and 20.09 hours. Altogether, therefore, 250 mg. of bemegride and 75 mg. of amiphenazole were given. After the second injection the patient made swallowing movements and sighed deeply. After the third injection he became more alert and turned his head. After the fourth injection his eyelids began to twitch. After the fifth injection, at 20.09 hours, he awoke and could talk a little, but his speech was slurred. Recovery progressed, and at 20.30 hours he was fully awake and aware of having been poisoned by tablets. In the night preceding November 22 he showed motor agitation, sprang out of bed, and had pronounced visual hallucinations. He calmed down after an injection of 50 mg. of chlorpromazine.

In the morning of November 22 he was drowsy, but answered adequately when spoken to. He was, however, a good deal more drowsy than after the bemegride and amiphenazole injections on the previous evening. He required no more stimulants but brightened up later. During the further course pleuropneumonia supervened, which was treated with antibiotics; there were no other complications. The patient was transferred to a mental hospital after staying in this hospital for ten days.

Examination on November 28 showed: W.B.C., 5,600 (polymorphonuclear 54%, "stab" cells 2%, eosinophils 1%, basophils 0%, lymphocytes 37%, monocytes 6%); thrombocytes, 173,000 per c.mm.; prothrombin according to Quick-Lehmann, 96; residual nitrogen, 30 mg. per 100 ml.; Meulengracht, 1:3; Takata-Ara, negative.

GERHARD DOTEVALL, M.D.,
BIRGER HERNER, M.D.,
Department of Internal Medicine,
Varberg Hospital, Sweden.

REFERENCES

- Arnold, O. H., and Ceranke-Höfermayer, S. (1953). *Wien. med. Wschr.*, 103, 692.
Morley, D., and Wynne, N. A. (1957). *British Medical Journal*, 1, 90.
Sciarrà, D., Carter, S., Vicale, C. T., and Merritt, H. H. (1954). *J. Amer. med. Ass.*, 154, 827.

Acute Epidemic Myalgia of the Hip

During the five months August to December, 1955, a series of cases were seen in the neighbourhood of Heatherwood Orthopaedic Hospital all showing a similar clinical picture—that is, severe pain in the hip, with limitation of movement. Most of the cases were pyrexial. Children and adolescents were mainly involved. A characteristic of the illness was early recovery following rest, and it left no after-effects. Eight of the cases were seen by me personally, and the histories and follow-up of six other cases were kindly supplied by Dr. E. V. Lambert.

All these cases were seen during the poliomyelitis epidemic of 1955 (see Chart), and in seven cases poliomyelitis was first diagnosed. Other diagnoses made initially were osteomyelitis in two cases, suppurative arthritis in one case, and some form of trauma in four cases.

The age range of the patients was 3½ to 35 years (average 12.8 years), only one being over 20. The sex distribution was eight males and six females. The right hip was affected in eleven cases and the left in three.

The commonest initial diagnosis was poliomyelitis, and this was suggested by the history of being off-colour for one to seven days, pain in the leg, and in the majority of cases a temperature up to 105° F. (40.6° C.), in some of them associated with coma, vomiting, and frontal headaches. The diagnosis of an infective lesion made in three cases was suggested by a raised sedimentation rate, a raised white-

cell count in two, and severe pain. Those cases thought to be due to injury had given some history of injury prior to admission which it was thought might have accounted for the symptoms. In all cases where x-ray pictures were taken, these were normal. In all cases except

Seasonal occurrence of poliomyelitis and acute myalgia in 1955.

one the symptoms were severe enough to justify admission to hospital. One patient was seen at home, and the symptoms were settling with rest in bed. The average stay in hospital of the other cases was just under 14 days. All patients had made a full recovery in a month, and a follow-up at nine months showed no recurrence of any symptoms.

The outstanding symptoms in these cases were: pain in 14 cases, spasm in 14, pyrexia in 10, and raised E.S.R. in 5. In the majority there was marked spasm in the hip when it was moved. In all cases a few degrees of passive movement could be obtained which was painless.

COMMENT

The clinical picture in these cases suggests that some infection was occurring during the months of August to December, 1955, causing an acute myalgia which seemed to single out the muscles in the region of the hip-joint and mainly affected children and adolescents. It ran a course lasting about two weeks and then subsided completely. In the majority of cases a raised temperature and other general reactions were noted.

From this description one would have to consider a virus infection as being the cause, and the fact that it coincided with a fairly severe epidemic of poliomyelitis during the same season of the year suggests that the virus may have been related—such as a Coxsackie infection (see Chart).

Coxsackie infection was first described by Daldorf and Sickles in 1948. Since then further work has shown that it is the cause of Bornholm disease (epidemic pleurodynia, epidemic myalgia), and herpangina.

It is an acute febrile, self-limiting, infectious disease affecting children and young adults, and in the above conditions the virus has been isolated from the stools or throat.

No specific treatment is available. The disease appears to be widespread and has been reported from most of the countries of the world. It occurs most frequently during the poliomyelitis season and is sometimes found coincidentally in patients suffering from poliomyelitis. It has been shown to be spread by sewage and flies, and is highly infectious—often involving several members of one family. Many may carry the virus without showing any clinical signs of the disease.

I have been unable to find any description in the literature of acute myalgia affecting the hip region, but the present cases were all similar in that they occurred during the poliomyelitis season; the main feature was acute pain; while the condition cleared up completely, leaving no after-effects.

I am grateful to Dr. E. V. Lambert for providing clinical notes of his cases. From the six cases that he had seen he had independently come to the conclusion that these cases were probably due to a Coxsackie-like virus infection.

G. P. ARDEN, M.B., F.R.C.S.,
Heatherwood Orthopaedic Hospital.

REFERENCE

- Daldorf, G., and Sickles, G. M. (1948). *Science*, 108, 61. Quoted by A. Beeman, *Practitioner*, 1954, 173, 551.