with 0.6 g. of thiouracil daily for 20 days, and was then given a maintenance dose of 0.2 g. daily for a week. She was discharged from hospital feeling very well. Her weight had increased by half a stone in a month, and her B.M.R. had fallen from +55 to +8. A mild tachycardia was the only residual sign of her thyrotoxicosis. She was told to continue to take 0.2 g. of thiouracil daily, but owing to a misunderstanding she actually took 0.4 g. As her home was in the far North of Scotland it was impossible for her to report to us regularly, and she was seen once a month by her own doctor. The first three reports from him were most satisfactory, but the fourth stated that she was not quite so well, though no specific symptom was noted beyond some lack of energy. By the fifth month this symptom had become pronounced, and a swelling of the neck was reported. The patient was immediately sent for, and on readmission, five and a half months after her discharge, was found to have a very large soft goitre. This was associated with a mild degree of myxoedema. Her weight had increased by one stone since discharge from hospital, her B.M.R. had fallen to -20, and her blood cholesterol had risen from 220 to 266 mg. per 100 c.cm. Her white blood count of 5,600 showed no significant alteration. Thiouracil was immediately stopped, and in two weeks' time she felt considerably better, her B.M.R. having risen from -20 to -3. No change had occurred, however, in the size or consistency of the goitre, and thyroidectomy was undertaken, principally for cosmetic reasons. At operation the thyroid was obviously enlarged, and was firm though not hard. The cut surface was typical of the hypertrophy associated with a primary toxic goitre which had not been treated by iodine. A section of the gland is shown in the accompanying photomicrograph. It can be seen that

there is extreme parenchymatous hyperplasia and an almost complete absence of colloid, the picture being similar to that produced by Mackenzie in animals treated with goitrogenic substances. After the operation the patient made an uninterrupted recovery, and was discharged home feeling well.

Comment

It is thought worth while to record this case as providing another instance to those noted by Himsworth of thiouracil causing a great enlargement of the goitre in a previously thyrotoxic patient. It gives practical proof of the theoretical assumption that if the pituitary is stimulated to produce excess thyrotrophic hormone by overdosage with thiouracil an increase in the size of the goitre will occur similar to the hyperplasia of the thyroid produced in experimental animals by thiourea and its derivatives, and by sulphaguanidine. A rapid and significant enlargement of the goitre in a patient under treatment with thiouracil may thus be evidence of overdosage.

REFERENCE

Himsforth, H. P. (1944) *Proc. roy. Soc. Med.*, **37**, 693.

Medical Memoranda

A Method of Administering Systemic Penicillin

Owing to the shortage of rubber tubing systemic penicillin is being administered by 3-hourly intramuscular injections, and it has been found that a good many patients complain of the pain and discomfort, and "come to dread the needle." The following method has been adopted and found satisfactory.

Pressure-tubing, outside diameter $\frac{1}{4}$ in., length $\frac{3}{4}$ in., is worked over the intramuscular needle and a glass cap applied to seal off (Fig. 1). The intramuscular needle is fixed in a suitable site with elastoplast strapping. Another strip of elastoplast is applied over the first, the projecting rubber tubing with glass cap is wrapped in sterile gauze, and the elastoplast is fixed in place. 15,000 units of penicillin in 1.5 c.cm. are drawn up into an all-glass syringe, and the needle removed. The nozzle of the syringe is inserted into the rubber tubing, which is steadied by forceps, injection given, and a sterile glass cap applied. Sterile gauze is wrapped round and elastoplast is reapplied (Fig. 2). The intramuscular needle can remain in place for four days without changing to a new site.

FIG. 1

FIG. 2

I wish to thank Mrs. W. K. Somerton for the illustrations, Mr. Garner of the pathological department for the suggestion of the glass cap, and Dr. Shepherd, the medical superintendent, for permission to publish.

Barnsley Hall Emergency Hospital.

H. L. MILLES, M.R.C.P.

A Case of Meningococcal Meningitis Treated with Penicillin

Since little is at present known about the effect of penicillin in meningococcal infections this case is considered worth recording.

CASE RECORD

A male child aged 18 months was admitted with a four-days history of repeated vomiting after all feeds. Previously he had been quite well. On the day before admission his mother had noticed that he felt hot and had a rash on his chest. There was no urinary retention and the bowels were normal. He had had gastro-enteritis at 2 months and at 6 months of age. The gain in weight had been good. On examination the child looked ill, being pale and lethargic. The anterior fontanelle was closed. There was slight diminution of skin elasticity. Some fading petechiae could just be seen on the thorax. The posterior cervical muscles were rigid, opisthotonos was

present, and a positive Kernig's sign and Brudzinski's neck sign were found. The C.N.S. showed normal cranial nerves and reflexes apart from absent abdominals. No abnormality was detected clinically in the chest, cardiovascular system, abdomen, throat, or eardrums, and the urine was normal.

Lumbar puncture on admission revealed a turbid C.S.F. under pressure: cells, 600 per c.mm., of which 66% were polymorphs; protein, 100 mg. per 100 c.cm.—globulin test positive; sugar, present but reduced; chlorides, 680 mg. per 100 c.cm. Microscopy showed numerous extra- and intra-cellular diplococci. Culture yielded a pure growth of *N. meningitidis* which proved sensitive to penicillin and sulphonamides. A blood count done at the same time showed R.B.C. 4,650,000 per c.mm., Hb 12.5 g.%, W.B.C. 16,200 per c.mm., of which polymorphonuclear cells comprised 59%, lymphocytes 29%, and monocytes 12%.

Shortly after being admitted the child had a convulsion and was comatose. As an alternative to intramuscular sulphonamide a request was made for penicillin. This was supplied and an intramuscular drip set up containing 67,500 units in 16 fl. oz. of 0.9% saline. The temperature was then 101.5°, pulse 122. Overnight the temperature rose to 103°. Owing to poor absorption only 23,000 units were given in the first 24 hours after the drip was started. During the second period of 24 hours 112,000 units were given, made up in 0.45% saline, about 8 fl. oz. being used. The patient was now taking fluids by mouth. At this time the urine contained acetone and reduced Benedict's reagent fully.

Seventy-two hours after the start of penicillin administration (202,500 units absorbed) the rectal temperature was 99.5° and the child had so much improved that he recognized his parents and took hold of toys offered to him. Neck rigidity, though still present, was less marked. A second lumbar puncture showed a clear specimen, with cells 120 per c.mm. and chlorides 735 mg. per 100 c.cm. Culture yielded no organism, and the C.S.F. inhibited growth of the standard Oxford strain of staphylococcus.

Sulphamezathine was now given orally (0.5 g., 6-hourly), but ten hours later the temperature rose to 104°. A further course of penicillin was then started, 202,500 units being given during the next three days. By this time the temperature had fallen to 99° (rectal) and the child was able to walk about his cot, appearing normal in every way. He has since made an uneventful recovery. Total penicillin, 405,000 units in 6 days.

COMMENT

While under normal circumstances penicillin given intramuscularly does not enter the C.S.F., the observations in this case suggest that in the abnormal conditions of meningitis it may do so. It is evident that the dose given in the first 24 hours was inadequate. Penicillin should have been continued after 72 hours without a pause.

The continuous intramuscular drip was employed for the following reasons: (1) steady maintenance of blood level; (2) little disturbance of patient—0.1% novocain was included in the drip; (3) more numerous sites available. The daily dose was made up every 24 hours. A fresh drip apparatus was used each day, the whole being assembled complete with needle and then sterilized immediately before use. The outer sides of the left and right thighs were used alternately, the skin being cleansed with 2% C.T.A.B. and flavine in spirit.

I am indebted to Dr. Stanley Wyard, senior physician, and to Dr. Richard Hollick, R.M.O., for permission to publish this case.

GEORGE H. TEE, M.R.C.S., L.R.C.P.,
House-physician, Victoria Hospital for Children, Chelsea.

A Case of Weil's Disease Treated with Penicillin

The following record of a case of Weil's disease has two points of interest. The first is the clearing of the leptospira from the urine after only 6 injections of penicillin, coincident with rapid clinical improvement; the second, the demonstration of leptospira in the blood and urine on the day that the agglutination titre was as high as 1 in 1600.

CASE HISTORY

A private soldier aged 38 was invalided from France with pyrexia of six days' duration and reached this hospital on the evening of Sept. 12, 1944.

The patient reported sick on Sept. 7, complaining of a severe frontal headache and a sensation of chilliness and shivering. His temperature was 102.8° F. Next day he complained of generalized aching and soreness of the eyes. His conjunctivae were injected and his temperature was now 103° F. His liver was palpable and tender, and he vomited continuously. His blood was negative for malaria parasites and *Leptospira icterohaemorrhagiae*. There was a mild leucocytosis of 12,800. He was evacuated by air on Sept. 11, and the last entry on his medical card stated that his general condition was poor.

Clinical examination on arrival at the hospital showed that he was now lightly jaundiced and his conjunctivae were heavily injected. He stated that during August he had bathed frequently in a rat-infested river. On the 13th, examination of his urine revealed the presence of large numbers of spirochaetes morphologically identical with *L. icterohaemorrhagiae*. Blood was taken for the agglutination test and a few drops were examined by dark-ground illumination. Surprisingly, leptospira similar to those in the urine were

easily found. Later the report from Prof. Gardiner, of Oxford, stated that the serum was positive for agglutination of *L. icterohaemorrhagiae* to a titre of 1 in 1600.

Penicillin therapy was started at 6 p.m. The dosage was 20,000 units intramuscularly three-hourly until Sept. 17 and then four-hourly until it was stopped on the 20th. The total dosage was 900,000 units. Before the penicillin was begun the patient complained of a marked degree of general malaise. The following morning he said he felt all right and thought himself fit enough to get up. However, his temperature did not become normal until the 16th. Leptospira could not be demonstrated in his urine or blood from 9 a.m. on the 14th onwards. Specimens of his urine were examined daily until the 30th, and in none of them was the organism discovered. The patient did not develop any after-fever, and was discharged perfectly well on Sept. 30.

A. E. CARRAGHER, M.B., D.P.H.,
Assistant Lecturer in Pathology, Welsh School
of Medicine, and Pathologist
to Llandough Hospital.

Internal Hydrocephalus complicating Pneumococcal Meningitis Treated with Penicillin after Sulphonamides

Internal hydrocephalus is a well-known complication of post-basic meningococcal meningitis, but the following case shows that when the clinical course of the disease has been considerably prolonged by therapeutic measures it can arise also in infections due to the pneumococcus.

CASE REPORT

A male infant aged 2 months was admitted to hospital, having been unwell for a few hours, during which he had one convulsion. On examination he was found to be extremely ill, vomiting brown material, and grossly dehydrated. His temperature was 100.6° F., pulse uncountable, and respiration rate 40 a minute. No clinical signs were found in his chest or the central nervous system, but the C.S.F. was turbid and contained Gram-positive diplococci. On culture a pneumococcus was isolated which proved lethal to mice.

Subcutaneous saline was administered and 0.5 g. of sulphapyridine by mouth every four hours, but after 5.5 g. had been given this was stopped on account of persistent vomiting. This treatment was accompanied by a fall in the temperature to 97° F., but next day, the fourth after admission, it rose to 101.4°. Sulphathiazole was then administered in the same dosage, but starting with 1 g. The temperature did not settle and the infant remained very ill. On the seventh day 10,000 units of penicillin were injected into the right lateral ventricle, after which 2,000 units were given intramuscularly every four hours. By the ninth day the C.S.F. contained only a few cocci; these were avirulent to mice. On the next day the temperature became steady at a normal level. The child's general improvement was pronounced, and no more organisms were recovered from the C.S.F. On the seventeenth day he became unwell again, and developed attacks of twitching with cyanosis and some vomiting. No C.S.F. could be obtained from the spinal canal in the lumbar region, but that in the basal cisterns was under raised pressure. It contained 600 mg. of protein per 100 c.cm. and 60 lymphocytes per c.mm.; no organisms were seen in it, and cultures were sterile. The child died two days later, on the twentieth day after admission, the illness having lasted for 21 days altogether.

Findings at Necropsy.—Nothing abnormal was found outside the central nervous system. The brain was fixed by withdrawing fluid from the cisterns and ventricles and replacing it with formalin 24 hours before opening the skull. Films of this fluid showed effete polymorphs, some of which contained degenerate-looking Gram-positive cocci. Cultures of the C.S.F. were again sterile. Many adhesions were present between the pachy- and lepto-meninges, and a dense fibrinous exudate surrounded the brain stem and filled the cisterns. All the cerebral ventricles were markedly dilated down to and including the fourth. They all contained turbid fluid and fibrin coagula. In histological sections of the meninges the exudate was seen to contain many polymorphs. The choroid plexus was covered with a similar exudate, but this contained many Gram-positive cocci as well.

DISCUSSION

Death was caused by internal hydrocephalus due to the fibrinous exudate. In their series of 16 cases of pneumococcal meningitis treated with penicillin Cairns, Duthie, Lewin, and Smith (1944) had one case of obstruction of the aqueduct of Sylvius, but this was apparently due to pressure of an abscess. Evans (1944) saw no such condition in his small series of cases of purulent meningitis. The likelihood of the development of such a fibrinous exudate in the early stages of the infection would seem to be another reason for treating all cases of pneumococcal meningitis with penicillin as early as possible—a procedure already recommended by Cairns *et al.* in their paper.

I have to thank my colleague Dr. P. Forgacs, under whose care the child was, for his co-operation.

Department of Pathology,
Guy's Hospital Medical School. R. E. REWELL, M.D., M.R.C.P.

REFERENCES

- Cairns, H., Duthie, E. S., Lewin, W. S., and Smith, H. V. (1944). *Lancet*, 1, 655.
Evans, A. L. (1944). *J. Amer. med. Ass.*, 124, 641.