therefore often called "resistant rickets or osteomalacia." Treatment, first in the form of pure dihydrotachysterol and then of A.T.10, cured the symptoms, raised the plasma phosphorus level (and presumably the renal threshold for phosphate ion), established a large positive calcium balance, and led to calcification of the Looser zones. With treatment the plasma alkaline phosphatase value also fell to normal, to rise again only during pregnancy; even then it did not rise above the level considered normal for pregnancy by Beck and Clark (1950). It had returned almost to normal a week after delivery. The excellent clinical response occurred in spite of the customary statement on the bottle of A.T.10 that "this substance has no antirachitic action." The current view in this laboratory is that dihydrotachysterol has excellent antirachitic action in the human subject and can be considered in every way as a form of vitamin D. No alkali was given and the degree of acidosis remained unchanged throughout, indicating that the acidosis is not the cause of the bone changes.

The diagnosis was made by Dr. Kellock and the patient subsequently treated by us before any significant deformities had occurred, so that after treatment she had no residual disability. Her pelvis was obstetrically satisfactory and her labour uneventful.

Early diagnosis and treatment can hardly be more rewarding, and their advantages need no further stressing. Failure to diagnose and treat this condition, however, results in rapid progression with development of deformities which are crippling (Dent and Harris, 1956) and irreversible.

It is not yet clear whether this type of adolescent osteomalacia is inherited. There was certainly no family history in this case. Even if the infant of an affected mother should develop the same disease in adolescent life, it would still probably be normal at birth and for the first few years of life. In the present case there was the further danger, however, that the treatment of the mother with dihydrotachysterol might affect the infant by causing a hypercalcaemia. The first analyses of the plasma of the infant were therefore awaited with some anxiety, and the cord blood, when obtained, showed a high calcium and low alkaline phosphatase content, suggesting a degree of vitamin-D intoxication. Hallman and Salmi (1953) have, however, shown that blood plasma travelling from the placenta to the foetus has a calcium content of 11–13 mg. per 100 ml. Clinically the infant thrived, and a week later its plasma values were normal. Its progress will now be followed with great interest and less anxiety.

It was considered highly undesirable that the mother should breast-feed the infant, since this would presumably greatly alter the calcium metabolism and consequently affect the requirement of A.T.10. Lactation was therefore suppressed by the method in routine use at the Obstetric Hospital.

The basic aetiology of this condition remains obscure, and no new suggestions are put forward here. The object of this paper is to describe the condition and to indicate how beneficial are the results of early diagnosis and therapy, even when there is the added strain of pregnancy.

Summary

A case is described in which a healthy adolescent girl suddenly developed renal tubular osteomalacia. She also showed some of the metabolic features of vitamin-D deficiency. These were reversed by oral administration of pure dihydrotachysterol and later A.T.10, resulting in rapid clinical and radiological improvement. Early therapy, before the development of deformities, resulted in complete functional cure, and she was able to sustain a normal pregnancy, labour, and delivery within 12 months of her first admission to hospital.

I wish to thank Dr. C. E. Dent for permission to publish this case and for his encouragement in the preparation of this paper.

My thanks are also due to Professor W. C. W. Nixon for supervising the patient's pregnancy and delivery, and to Messrs. Merck (Darmstadt) for a gift of pure crystalline dihydrotachysterol.

REFERENCES

- Albright, F., Butler, A. M., and Bloomberg, E. (1937). *Amer. J. Dis. Child.*, **54**, 529.
 — and Reifenstein, E. C. (1948). *The Parathyroid Glands and Metabolic Bone Disease*. Williams and Wilkins, Baltimore.
 Beck, E., and Clark, L. C. (1950). *Amer. J. Obstet. Gynec.*, **60**, 731.
 Dent, C. E. (1952). *J. Bone Jt Surg.*, **34B**, 266.
 — and Harris, H. (1956). *Ibid.*, **38B**, 204.
 — and Hodson, C. J. (1954). *Brit. J. Radiol.*, **27**, 605.
 Hallman, N., and Salmi, I. (1953). *Acta paediat. (Uppsala)*, **42**, 126.
 Jackson, W. P. U., and Linder, G. C. (1953). *Quart. J. Med.*, **22**, 133.
 Leedham-Green, J. C., and Golding, F. C. (1937–8). *Brit. J. Surg.*, **25**, 77.
 Le May, M., and Elunt, J. W. (1949). *J. clin. Invest.*, **28**, 521.
 Liu, S. H., and Chu, H. I. (1943). *Medicine*, **22**, 103.
 Looser, E. (1920). *Dtsch. Z. Chir.*, **152**, 210.
 McCance, R. A. (1947). *Quart. J. Med.*, **16**, 33.
 Michaelis, L. (1932). *Fortschr. Röntgenstr.*, **45**, 187.
 Monier-Vinard, R. (1940). *Bull. Soc. méd. Hôp. Paris*, **56**, 529.
 Steinbach, H. L., Kolb, F. O., and Gilfillan, R. (1954). *Radiology*, **62**, 388.

Medical Memoranda

Acute Haemorrhagic Leuco-encephalitis

Few cases of this condition have been reported since Weston Hurst (1941) described two cases of fatal encephalitis with specific macroscopic and microscopical appearances of the brain, which he named "acute haemorrhagic leuco-encephalitis." The disease consists of an encephalitis of acute onset, which is usually but not necessarily preceded by a prodromal upper respiratory infection. This is followed in some cases by a period of apparent recovery, before the onset of neurological symptoms leading to coma. In the cases reported the prodromal period had varied from 0 to 15 days, the intervening period from 0 to 11 days, and the neurological stage from 2 to 6 days, terminating fatally.

Post-mortem examination of the brain shows lesions confined almost entirely to the white matter of one or both cerebral hemispheres, but these may extend to the white matter of other parts of the brain. Some parts show only microscopical involvement. Macroscopically there are haemorrhages varying in size from pin-point up to a few millimetres in diameter. They are confined almost solely to the white matter and are associated with oedematous swelling of the adjacent tissues. Microscopically there are characteristic lesions: (1) perivascular ring and ball haemorrhages; (2) serous exudates; (3) perivascular polymorphonuclear exudates; (4) focal and perivascular demyelination; and (5) vascular degeneration with replacement of the wall by fibrinoid material, fibrinoid material in the lumen, and perivascular tissues.

Detailed descriptions of both macroscopic and microscopical lesions are given by Hurst (1941), and by Crawford (1954) in a paper reviewing the cases published to date. The aetiology is unknown.

CASE REPORT

A shop assistant aged 19 was admitted unconscious into hospital on February 9, 1955. The clinical history was taken from the parents and the general practitioner's letter. This girl developed acute glomerulonephritis at the age of 16. She was investigated and treated at the London Hospital. The nephritis became chronic. At the follow-up attendances albumin in the urine, moderate oedema of the ankles and legs, and a normal blood pressure were found.

About the middle of January, 1955, she developed a simple cold and a loose cough with moderate amounts of white sputum. Her condition improved, but nine days before admission she developed a temperature and left-sided

pleuritic pain, which subsided in two days with chlortetracycline (1 g. daily for four days). Three days before admission she felt less well and in the evening developed intense headache, nausea, and vomiting, which persisted until the onset of coma. The doctor examined her the following morning. Her temperature was 103° F. (39.4° C.) and pulse 100. She had mild photophobia, but no neck stiffness was present. Chlortetracycline was recommenced. On the morning of admission she was semiconscious and very restless and had been incontinent of urine.

On admission the patient, a well-built girl, was unconscious and extremely restless. She was picking at her lips and nose. Her temperature was 98.4° F. (36.9° C.), pulse 80, and respirations 20. She was incontinent of urine. There was no skin rash. She had conjugate deviation of the eyes to the left. The pupils were dilated and did not react to light. Nothing abnormal was seen in the optic fundi. There was trismus. The teeth appeared to be normal. The

Photograph of section taken from white matter of right occipital lobe. Stained with haematoxylin and eosin.

tongue, so far as could be seen, was coated and moist. There were sordes on her lips. Both eardrums appeared normal. The lungs were clinically normal. The pulse was regular and the blood pressure 160/90. A soft mitral systolic murmur was heard. There was no sacral or ankle oedema and the jugular venous pressure was not raised. A corneal reflex was present on both sides. The reflexes and tone in both arms were normal. The abdominal reflexes were absent. The reflexes and tone in both legs were increased. There was ankle clonus. The left plantar response was extensor. Neck rigidity, mild opisthotonos, and a positive Kernig's sign were present. The patient failed to respond to nociceptive stimuli on the left side of the body. A provisional diagnosis of pneumococcal meningitis was made.

Lumbar puncture showed a pressure of over 300 mm. and 5 ml. of slightly yellow opalescent fluid was removed, crystalline penicillin (20,000 units) was injected into the theca and 2 g. of sulphadiazine was given intravenously, followed by 2 g. intramuscularly every four hours.

Despite treatment she lapsed into deeper coma. The corneal reflexes were unobtainable and the arms and legs became flaccid. A gallop rhythm was heard over the praecordium. The patient died 17 hours after admission.

Investigations.—C.S.F.: pressure, 300+ mm.; cells, 2,000 (polymorphs 90%); protein, 620 mg./100 ml.; chlorides, 720 mg./100 ml.; sugar, 80 mg./100 ml.; no organisms seen on direct examination. The 24-hour culture was sterile. Post-mortem blood urea, 124 mg./100 ml. The urine contained albumin.

Post-mortem Examination.—Apart from the kidneys and brain, nothing abnormal was found. The kidneys were enlarged one and a half times by thickening of the cortex,

which was a pale yellow colour with some red streaking. There was a thin layer of subarachnoid haemorrhage round the mid-brain, especially in the cerebro-pontine angles. The vessels of the circle of Willis and its branches were not obstructed. There was a large area of ischaemic softening involving almost the whole of the right occipital lobe. Finger-like processes of a similar nature extended along the wall of the lateral ventricle on both sides, especially at the junction of the lateral, posterior, and inferior horns, and the hippocampus. The right basal ganglia were similarly softened and there were isolated zones in the right parietal white matter and in the mid-brain.

Histological examination of the white matter of the right occipital lobe beyond the edge of an area of softening showed lesions of a patchy nature separated by brain tissue which was apparently normal. The affected parts were centred on blood vessels, particularly the small venules. These showed a curious loss of structure of the vessel wall which was converted into the structureless eosinophilic material usually described as "fibrinoid," and, although the endothelium was absent and the fibrinoid material somewhat fragmented, there was no effusion of red corpuscles through the wall. Polymorphs, however, were present in large numbers in the lumen, in the wall, and in the tissue surrounding the vessels. Capillaries were hardly affected, but small flame-shaped and ring-shaped haemorrhages were seen (see Fig.), the latter surrounding small areas of necrotic brain tissue. Serous exudate was not found in the sections examined, but fibrinoid material appeared to have diffused out of most of the damaged vessels in the surrounding tissue.

I wish to thank Dr. G. R. Steed for advice and permission to publish this case, and Dr. M. R. Thomas for performing the necropsy and preparing the histological sections.

H. E. ALDRIDGE, M.B., B.S.,
Late House-physician,
South Devon and East Cornwall Hospital, Freedom Fields.

REFERENCES

- Crawford, T. (1954). *J. clin. Path.*, 7, 1.
Hurst, E. W. (1941). *Med. J. Aust.*, 2, 1.

Case of Acute Haemorrhagic Leuco-encephalitis

Acute haemorrhagic leuco-encephalitis is a rapidly fatal disease of the central nervous system in which haemorrhagic lesions are found in the white matter of the brain. Crawford (1954) described three cases and found a further seven in the literature up to that time. Adams, Cammermeyer, and Denny-Brown (1949) described four similar cases under the name of acute necrotizing haemorrhagic encephalopathy.

Clinical Description.—The condition is commonest in young adults, but the youngest in Crawford's series was aged 2 years 10 months, and the oldest reported case was aged 51. It is commoner in males than in females. In most cases an acute upper respiratory infection precedes the neurological signs by a few days. The latter are acute in onset, with high fever, neck rigidity, sometimes convulsions, and paralyses with no characteristic distribution. The onset of coma is early and death follows in a few days. The cerebrospinal fluid usually shows an increase in cells, the maximum in Crawford's series being 220 per c.mm., but Adams *et al.* reported up to 5,000 per c.mm. Most of the cells are polymorphs. The protein is slightly increased in about half the cases; it was 140 mg. per 100 ml. in one of Crawford's. The sugar and chlorides were normal in three cases. Those cases in which the blood count was recorded showed a polymorphonuclear leucocytosis.

Pathology.—The meninges may appear normal or congested. The convolutions are flattened. The cut surface of the brain shows one or more pinkish oedematous areas, with numerous small haemorrhages of varying size, not more than a few millimetres in diameter, scattered through the white matter. The distribution is usually mainly in the cerebral white matter of either or both sides, often asym-