occupations, such as that of a clerk, or whether such occupations themselves lead to any particular form of heart weakness. This point can only be decided by a detailed examination of the incidence of the various forms of cardiac derangement in the various occupations. An attempt to do this will be made later.

EPIDEMIC POLIOENCEPHALITIS. (SO-CALLED EPIDEMIC BOTULISM.)

BY

CHARLES H. MELLAND, M.D. LOND., M.R.C.P.,
ASSISTANT PHYSICIAN, MANCHESTER ROYAL INFIRMARY.

PART I.

DURING the last five or six months I have seen a number of cases in which paralysis of some of the cranial nerves has been a prominent feature. The cases have been sufficiently numerous, indeed, to warrant the application of the term epidemic. It has been suggested by Professor Hall, of Sheffield, and others in the lay and medical press, that these are, or may be, cases of "botulism," a disease which has been attributed to the eating of food—particularly uncooked ham and sausage—infected with the *B. botulinus*. It is conceivable that the bacillus may effect a lodgement in the alimentary tract without producing any definite gastro-intestinal symptoms, and that the toxin there produced, circulating in the blood, might select for attack certain cranial nerves as does the toxin of diphtheria. But there is little, if any, evidence to connect the recently recorded attacks with any special articles of diet, and the epidemic, in its widespread character, does not resemble that usually associated with poisonous food, but rather suggests the type associated with symptom-free carriers, as is almost certainly the case in poliomyelitis, and in cerebro-spinal fever.

I had, indeed, concluded in my own mind that I had to deal with an epidemic of infective polioencephalitis, using that term to designate an affection of cranial motor centres produced by the same elusive organism that gives rise to epidemic poliomyelitis, and I have expressed that belief in the title of this communication. A weak spot in this suggestion is perhaps the fact that I have not met with an undue number of cases of poliomyelitis, such as one would expect to be associated with an epidemic of polioencephalitis, nor has such frequency of poliomyelitis, I believe, been recorded. Further, the possibility of an access of botulism associated with the considerably increased consumption of tinned meats during the period of restricted supply of fresh meat must be kept in mind.

The following are the only cases which I have kept any available notes. The first does not belong to the present series since it is one that came under my observation over four years ago, but it is obviously a sporadic case of the same nature as those now epidemic.

G. M. P., a girl aged 12, was seen in the out-patient department of the Royal Infirmary on August 29th, 1913. She had had pain in the head for four days and "turning of the eyes" for three days. She had been sick the day before. She was taken to the Royal Eye Hospital, where she saw Dr. Clegg, and by him was sent on to the infirmary. There was then paralysis of the left sixth nerve, which gave rise to convergent squint, and she had marked optic neuritis. She was constipated. During the next fortnight she continued much the same; she was sick once and had pain in the head and also in the arms and back, and then it was noticed (September 12th) that she had right facial paralysis, though not complete. By September 19th this facial paralysis was well again, but on October 3rd, though there had been no further sickness or headache, she had facial paralysis on the left side. After this date she steadily improved; the paralysis gradually passed off, though there was partial atrophy of the left optic nerve.

I showed this patient at the meeting of the Neurological Society held in Manchester in May, 1914, as probably a case of cerebral tumour that had made a good recovery, but the general view of those who discussed the case was that it was one of polioencephalitis, and that the time of year at which it occurred lent support to this view, since August and September are the months in which poliomyelitis and polioencephalitis are most frequent and occasionally assume an epidemic form.

Of the more recent cases which fall into the epidemic group the following are brief notes:

CASE I.

A. S., a boy aged 16, sent to my out-patient department on November 22nd, 1917, by Dr. Senior of Levenshulme. He had been suffering from left-sided facial paralysis for about a week; he had noticed it first on getting up in the morning, and had attributed it to draught from the window at night. He had slight pain in the left side of the face. All the branches of the nerve, both the upper as well as the lower, were involved. In addition, there was paralysis of certain branches of both third nerves on both sides, the right internal rectus and both internal and external recti of the left eye being involved; there was no optic neuritis. There was little, if any, general disturbance. The paralysis got well in about another week—so rapidly, indeed, that Dr. Senior, who had at first feared cerebral tumour, was inclined to regard the condition as hysterical. Some weeks later he had a slight transient recurrence.

CASE II.

B. J., a boy aged 13, an out-patient at the Royal Infirmary, had facial paralysis on the right side, starting about December 20th, 1917. There was but little local pain or discomfort, and no general symptoms. There was no clue as to the origin of the paralysis. He very rapidly improved under the potassium iodide and sodium salicylate, and was discharged cured by February 21st.

CASE III.

G. T., a girl aged 12, seen in my out-patient department on March 28th, 1918, was taken ill about January 14th, 1918, with drooping of both eyelids and pains in the head, particularly at the back of the eyes. She had no vomiting, but had pyrexia, with some delirium and clouded consciousness. She was an in-patient in a cession at the Eye Hospital, the Royal Infirmary, and the Convalescent Hospital. When she came under my care on March 28th there was still some drooping of the eyelids, though they were better than they had been, and there was divergent squint due to paralysis of the left internal rectus. There was no optic neuritis in this case.

CASE IV.

I. A., a girl aged 14, seen in consultation with Colonel Coates on March 25th, 1918. She had some headache about Christmas, 1917, which was put down as probably the result of a fall on the back of the head shortly before. The headache continued off and on for some weeks, but latterly she had had no trouble with it to speak of. Five weeks back, however, she had begun to see double, and Dr. McNabb found that she had optic neuritis and paresis of the right external rectus. During the whole period during which she had the headaches she had not seemed well of herself, but had not been in any way acutely ill, and when I saw her in March, except for some degree of anaemia she appeared in her normal health. The optic neuritis is now (May 11th) clearing up, and the diplopia and paresis of the left external rectus are now well.

CASE V.

W. B., aged 21, came as an out-patient to the Royal Infirmary on April 4th, 1918. He had had a left facial paralysis, coming on without ascertainable cause about ten days previously. He improved very satisfactorily under treatment, and was discharged cured on May 2nd. He never showed any other local or general symptoms beyond the facial paralysis.

CASE VI.

A. C. W., aged 33, a signalman, seen in the out-patient department of the Infirmary on the same date as the above. He had had right facial paralysis, coming on without ascertainable cause, about eight days previously. He has failed to respond to treatment, and up to date (May 2nd) has made practically no improvement.

CASE VII.

E. C., aged 42, seen in the out-patient department at the Infirmary on April 11th, 1918. She had had weakness of the left eyelid coming on gradually for three weeks. She had had headache, but not very severe. On examination, there was complete ptosis on the side, with no affection of any other eye muscles; the pupils reacted normally, and fundi and fields were normal (Dr. J. G. Clegg). She has improved slightly, the droop of the left upper lid being somewhat less than it was; no further paralysis has developed.

CASE VIII.

M. C., aged 41, insurance agent, was sent to my out-patient department at the Infirmary on May 2nd, 1918, by Dr. Blake-more of Tyldesley, with a note suggesting "?commencing disseminated sclerosis." He started with right-sided facial paralysis six or eight weeks ago. He was unable to close his right eye and saw double. The facial paralysis has now practically recovered. He had also some slight drooping of the left eyelid, and this, after getting better for a while, had become worse. When seen there was well-marked ptosis. He still had double vision, and there was paresis of the right internal rectus and of both superior recti. There was no optic neuritis. He had had no general symptoms of illness, and, despite the difficulty of seeing clearly, he had continued at his work with assistance.

CASE IX.

M. M., aged 11, seen in consultation with Dr. Barnes of Fails-worth on April 28th, 1918. She had been ill for about fourteen days with pain in the head and mild pyrexia, about 100° F. The pain was mostly about the back of the head and neck, and there had been distinct stiffness of the muscles at the back of the neck. She had vomited once, and the tongue was dirty. There had been a good deal of general malaise, but when I saw her she was better and was sitting up in bed reading and anxious to be allowed up. There was no paralysis of any of the face muscles, nor any complaint of double vision, but she had well-marked double optic neuritis. On May 5th Dr. Barnes informed me that she had since complained of double vision, though there was no recognizable ocular paralysis. The optic neuritis is now beginning to clear up.

CASE X.

Mrs. W., aged 61, seen in consultation with Dr. McLean of Harpurhey on March 20th, 1918. She had had gradually progressive asthenia for two or three weeks with slow mentality and forgetfulness, and slight continued pyrexia. It was difficult to get her to answer any questions about herself, though after I had been with her for a time she roused up to a certain extent, and took some interest in my visit. There was no paralysis of cranial nerves then, and no optic neuritis, but she subsequently developed facial paralysis. She gradually got worse, and sank into a more and more confused and asthenic condition, and died about a fortnight later.

CASE XI.

Mrs. P., aged 62, also seen in consultation with Dr. McLean of Harpurhey on April 3rd, 1918. She had had symptoms of arterio-sclerosis—recurrent headache and dizzy attacks—for two or three years past. For some days before I saw her she had been suffering from headache, and had been dull and confused, and the day before sudden ptosis of the left eye had developed, and she had diplopia, due to fairly complete paralysis of all the straight muscles of the left eye. She complained of a good deal of pain and headache above the eye, made worse on examining for optic neuritis, which was absent. The urine was free from albumin. She had gradually improved, but on May 5th there was still some drooping of the left lid and diplopia.

With the exception of Mrs. W. (Case x) and of G. T. (Case III), the general symptoms have been comparatively slight, certainly not of the severity suggested by Professor Hall in his brief note of the cases he has seen in Sheffield. It would appear as if most of the cases I have seen were of a subacute type.

I have had some doubts as to whether the three cases of simple unilateral facial paralysis should be included, since they differed in no way from the sporadic cases with no ascertainable cause that are of fairly common occurrence. In view of their unusual frequency, however, and of the belief which I know is held by some physicians that facial paralysis is not uncommonly an expression of polio-encephalitis, I have thought well to retain them.

I have some doubts also of the exact nature of the two following fatal cases. In neither of them was there any cranial nerve paralysis, but the progressive asthenia and drowsiness, advancing to coma, without definite evidence of meningitis, have inclined me to believe that they fall into the same category. I may say that I have during the period come across (but not had under my own care) several cases of similar type, some of which have ended fatally, whilst others have got well after being in apparently a dying condition for some days.

CASE XII.

Mrs. N., aged 28, seen with Dr. Kenny of Pendleton on February 16th, 1918. She had started about February 12th with symptoms suggestive of a mild influenzal attack and a temperature of 100° F. On February 13th she was better, but on February 14th complained of headache and began to be drowsy, and when I saw her she was unconscious, though she showed that she could just feel firm nipping of the skin between one's finger nails. Her pulse was fast (120), breathing not faster than normal. There was nothing abnormal to be discovered in the heart, lungs, or elsewhere. The urine was normal. There was no paralysis, and no optic neuritis. Her state of coma steadily deepened, and she died a few days later.

CASE XIII.

L. W., aged 22, seen with Dr. Barnes of Fails-worth on March 19th, 1918. She had been ill for about a week, having started with chest symptoms—cough, rapid breathing, and pyrexia. For two or three days before I saw her she had been getting progressively more drowsy and weaker, and finally could not be roused at all. The urine was normal. There was no paralysis, no convulsions or twitching, but as I suspected tuberculous meningitis I took her into the Royal Infirmary under my care. Lumbar puncture yielded clear fluid under moderate pressure, which did not yield any pathological organisms on culture, and did not show the presence of tubercle bacilli or *Diplococcus intracellularis*. Her temperature remained high and

her coma gradually deepened till she died, two days later. The autopsy revealed purulent bronchitis and acute pulmonary emphysema, but there was no meningitis nor any recognizable naked-eye abnormality of the brain or meninges.

NEPHELOMETRIC ESTIMATION OF QUININE
IN BLOOD AND URINE.

BY

I. J. LIPKIN, M.B., CH.B., M.R.C.S., L.R.C.P.,

JOHNSTON FELLOW IN BIOCHEMISTRY,
AND

W. RAMSDEN, M.A., D.M.,

PROFESSOR OF BIOCHEMISTRY IN THE UNIVERSITY OF LIVERPOOL.

THE methods recorded below were devised, amongst others, in the course of work undertaken at the request of the Medical Research Committee. They are published at once in the hope that they will be useful to others who are investigating the treatment of malaria by quinine. A fuller account of these and other methods will appear in the *Annals of Tropical Medicine and Parasitology*.

By the following procedure estimates of small fractions of a milligram of quinine can be made with an error of less than 5 per cent. It has been found invaluable in dealing with such small amounts of the alkaloid as are contained in 5 c.cm. of human blood, when no other methods would have the necessary delicacy. It has also, by reason of its rapidity, proved very useful for approximate estimations of quinine in urine. Its success is due (1) to the great delicacy given to the Tanret turbidity test by using purified ether and by dissolving the quinine in saturated ammonium sulphate solution; (2) to the observation that comparisons of the opalescences of two suspensions can be made with greatly increased accuracy when the tubes are illuminated by a band of light admitted through a narrow adjustable slit.

Estimation of Quinine in Blood.

Five to ten cubic centimetres of blood are removed from the patient by a syringe, ejected at once into a weighed flask containing 2.5 to 5 grams of solid ammonium sulphate and 10 c.cm. of a saturated aqueous solution of this salt containing 0.6 per cent. H_2SO_4 , and the flask is re-weighed. Boil for two minutes, shaking all the time, and pour off the liquid portion while hot into a small Gooch crucible under suction. Catch the filtrate in a test tube and transfer it to a 50 c.cm. stoppered cylinder. Add 10 c.cm. more acidulated ammonium sulphate solution to the original flask, boil and filter as before. Wash the residue on the crucible twice with the hot filtrate before adding it to the original filtrate. Repeat the boilings with three further lots of acidulated ammonium sulphate solution, on each occasion washing the residue on the crucible two or three times. Cool the filtrate, alkalize it with strong ammonia and extract with four 7 c.cm. lots of purified ether (*v. infra*), removing each lot as it separates, and transferring it to one of a special series of test tubes gauged for nephelometry. Evaporate off the ether on a hot water bath, taking care to avoid loss by spurring—the tube now contains the whole of the quinine of the original blood. Control experiments with normal blood have shown that it contains no substance giving turbidity with Tanret's reagent. The test tubes are of thin-walled colourless glass, and have a diameter of about 13 mm. They are carefully selected so as to be equal in calibre in the lowest two centimetres of the cylindrical portion, this equality being ascertained by means of a suitably thick piece of glass tubing surrounded at its lower end by a half-centimetre length of thick black rubber tubing.

The nephelometer consists essentially of a well made dull-black parallel ruler, the lower bar of which is screwed horizontally to a wooden supporting open framework (for example, a photographic half-plate printing frame), which bears also a small shelf level with the lower edge of the ruler. By means of vertical cardboard screens light is blocked off from all but a middle portion of the slit two test tubes wide. The light should be strong. Between it and the slit is interposed a piece of opal glass or white semi-transparent paper. The ends of the test tubes rest on the transverse shelf referred to above, their sides are