CEREBRAL COMPLICATIONS OF CYANOTIC CONGENITAL HEART DISEASE

ROBERT MCDONALD, M.A., D.M., D.C.H. and FRANK HARRIS, M.B., CH.B.

Department of Child Health, University of Cape Town, and Groote Schuur Hospital, Observatory, Cape

Children with cyanotic congenital heart disease sometimes develop neurological complications. Cerebral abscess is one of them and is a serious condition, but if it is diagnosed and treated early, a cure is often possible. Cardiac surgery has advanced so much in recent years that it is tragic for a child with a potentially correctable heart lesion to die or be crippled as the result of neurological complications which may be amenable to treatment.

The case reports that follow are examples of some of these complications. The patients were seen in the paediatric wards of this hospital in recent years, and include those with cerebral abscess and vascular thrombotic lesions of both venous and arterial type. Although the symptoms and signs were similar in some patients, every effort was made to differentiate the conditions, since cerebral abscess, at least, offers a prospect of surgical cure.

CASE REPORTS

Case 1

A boy, aged 6 years, was seen on 6 June 1953. He had been blue since birth and had severe dyspnoea on exertion. Cyanosis, clubbing and marked polycythaemia accompanied a heart defect that was thought to be a Fallot's tetralogy. In hospital he developed fever, an increasingly severe headache, neck stiffness and a right facial weakness, and became irritable and drowsy.

Lumbar cerebrospinal fluid (CSF) was normal, but when a ventriculogram was attempted from the right side, three abscesses were struck from which yellow pus was aspirated. This pus showed gram-positive cocci on the smear only. Despite parenteral penicillin and streptomycin, and injection of these drugs into the abscess cavities, the CSF became frankly purulent and the child died 26 days after admission. There was no autopsy.

Summary. Multiple cerebral abscesses were found in a child with probable Fallot's tetralogy. Despite aspiration, a purulent meningitis developed which proved fatal.

Case 2

A girl, aged 7 years, with a history of cyanosis and fatigue on slight effort since the age of 1 year, was admitted on 30 August 1958, because of a severe right-sided headache for 10 days. Cardiac catheterization by Dr. M. Nellen when she was 4 years old had shown pulmonary atresia and a right-to-left shunt.

When seen in 1958, the clinical findings were consistent with the catheter diagnosis. She was polycythaemic, with a leucocytosis of 22,000 per c.mm., polymorphs predominating. Papilloedema, left-sided hemiparesis and slight neck stiffness were found, but the mental state was normal. The CSF pressure was 250 mm. H_2O with 68 cells, chiefly lymphocytes, per c.mm., but the chemistry was normal and no organisms were cultured. Blood culture was sterile. A carotid angiogram was normal but an electro-encephalogram (EEG) showed slow waves on the right side — a significant finding in view of subsequent events.

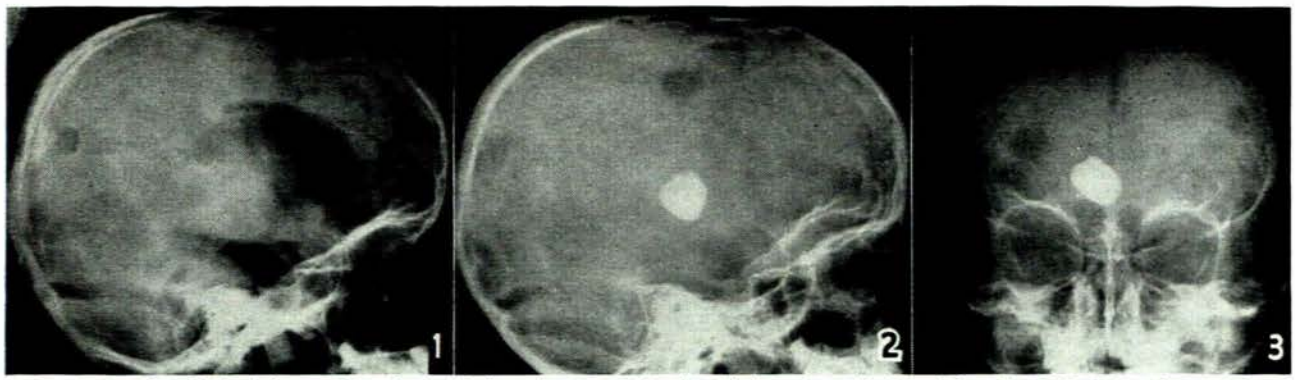

Fig. 1. Case 2 — Cerebral abscess shown by ventriculography, compressing the right lateral ventricle from below. *Fig. 2.* Case 2 — Abscess cavity outlined by 'thorotrast' (lateral view). *Fig. 3.* Case 2 — Abscess cavity outlined by thorotrast (A-P view).

Penicillin and streptomycin had been given from the time of admission, since a cerebral abscess was suspected: at first the child seemed to be improving, but by the third week in hospital her symptoms returned and increased in severity. A lumbar air encephalogram (AEG) done by Mr. A. Gonski filled only the left lateral ventricle, but a ventriculogram showed that there was considerable compression of the right lateral ventricle from below (Fig. 1). Needle aspiration of the right cerebral hemisphere yielded 25 ml. of pus at a depth of 7 cm., and penicillin, streptomycin and 'thorotrast' were injected. Further X-rays showed the outline of the abscess cavity (Figs 2 and 3).

The child's symptoms improved dramatically and there was a gradual and ultimately complete recovery from her neurological disability. Her cardiac defect, however, is considered inoperable at present.

Summary. A single cerebral abscess causing hemiparesis was found in a child with pulmonary atresia and a right-to-left shunt. Recovery from the hemiparesis occurred after drainage of the abscess. An EEG was of localizing value and ventriculography indicated the exact site of the abscess.

Case 3

A boy of 11 months, known to have cyanotic congenital heart disease, and with a history of attacks of vomiting for a month, was admitted on 11 August 1954, because of arching of the back and coma of sudden onset one hour previously. All his limbs were paralysed, but the optic fundi were normal. He was polycythaemic, and had a leucocyte count of 16,000 per c.mm., with 57% polymorphs. The CSF was normal. No radial pulsation could be felt in the right arm.

He did not recover consciousness, developed generalized convulsions with hyperpyrexia, and died on his third day in hospital. At autopsy there was thrombosis, some of it old, in the superior longitudinal sinus and cerebral veins, with cerebral softening, an embolus in the right radial artery and an infarct in the right kidney. The heart showed complete transposition of the great vessels and a ventricular septal defect.

Summary. A case of quadriplegia ending fatally in a child with transposition of the great vessels. Old and recent thrombi were present in the superior longitudinal sinus and cerebral veins. There was an embolus in the right radial artery and an infarct in the right kidney. Repeated vomiting may have resulted in dehydration in this polycythaemic child.

Case 4

A male baby of 17 months with a cardiac lesion thought to be Fallot's tetralogy was admitted on 21 March 1961. The child was found to have a right-sided hemiplegia and he also had pneumonia. He was extremely anaemic and had a leucocyte count of 21,000 per c.mm., with 71% polymorphs. The CSF was normal and the blood culture was sterile. After a blood transfusion cyanosis was seen to be present when the baby cried. Slow left-sided waves on EEG were in favour of cerebral abscess, but the AEG and a left carotid angiogram were normal.

Frequent cyanotic attacks developed, requiring morphine for their relief. Cardiac catheter studies supported the clinical diagnosis of Fallot's tetralogy. The cyanotic attacks decreased in severity, and cardiac surgery, at one time contemplated as a matter of urgency, has been postponed until the child is older. The hemiplegia has remained unchanged.

Summary. Hemiplegia caused by a non-suppurative cerebrovascular lesion occurred in a baby with probable Fallot's tetralogy.

Case 5

A girl, aged 14 months, known to have been cyanosed and short of breath from her earliest days, came to us on 21

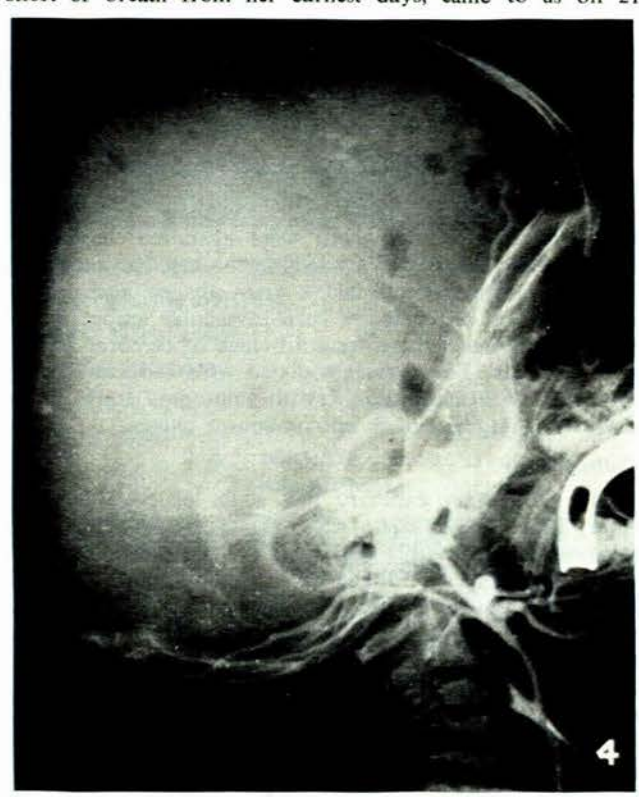

Fig. 4. Case 5 — Percutaneous carotid angiogram showing complete block of the internal carotid artery.

February 1961. Catheter studies by Dr. M. Nellen, some months previously, suggested a dextrocardia with a possible Fallot's tetralogy. On arrival, the child had a left hemiparesis with some papilloedema, which was especially marked in the left eye. She was polycythaemic, with a leucocytosis of 26,000 per c.mm., and a polymorphonuclear preponderance.

In spite of her age, a cerebral abscess seemed possible and chloramphenicol treatment was commenced. The CSF was normal, and since a lumbar air encephalogram was unsuccessful, the neurosurgeon (Mr. A. Gonski) followed this procedure by a percutaneous carotid angiogram on the right side. This showed a complete block of the internal carotid artery near its origin (Fig. 4). Cardiac catheterization suggested a dextrocardia and both great vessels seemed to be originating from the right ventricle. A ventricular septal defect was also thought to be present. Surgical intervention did not seem feasible and the baby was taken home.

Through the courtesy of Dr. Nellen we have learned that the child was later taken to London, where an operation of pulmonary valvotomy was performed, but she failed to survive this. Postmortem examination showed that there had been a severe pulmonary stenosis with transposition of the ventricles. The right carotid artery was completely occluded, resulting in gross atrophy of the cerebral hemisphere on that side, sparing only the temporal lobe.

Summary. Hemiplegia, caused by a carotid artery thrombosis, occurred in an infant with severe pulmonary stenosis and transposition of the ventricles.

DISCUSSION

Incidence

Cerebral abscess in congenital heart disease is said to be only half as common as non-suppurative cerebrovascular lesions.[1-3] The incidence varies from centre to centre, being 7% in a report from Bellevue Hospital, New York,[4] 3·1% from Baltimore,[5] but only 0·8% in a Toronto series.[6] In Minnesota, Cohen[7] found 3 cases of abscess in 100 autopsies on patients with congenital heart disease, while Ley *et al.*[8] saw only 2 cases in 15 years of neurosurgical practice in Madrid. Newton[9] reported 7 cases of cerebral abscess in children with cyanotic congenital heart disease over a 10-year period in Birmingham.

In Groote Schuur Hospital, 344 children with congenital heart disease, 147 of whom were cyanosed, have been admitted to the children's wards in the last 10 years. Two of the cyanotic patients had a brain abscess and 4 more suffered from an occlusive cerebrovascular lesion. In the period mentioned, there were 10 cases of cerebral abscess in our wards. Two were associated with congenital heart disease, 2 with mastoiditis, 2 with pulmonary suppuration, 1 with meningitis and 3 with unknown causes.

Pathogenesis

The pulmonary capillary bed is an efficient bacterial filter, but when a right-to-left shunt exists it is largely bypassed. Tyler and Clark[2] believed this fact to be of major importance in the production of cerebral abscess. Older writers suggested that the abscess develops at the site of lodgement of an infected paradoxical embolus. Groff[10] injected cats intracerebrally with virulent bacteria, but failed to produce abscesses unless the brain had previously been damaged. Berthrong and Sabiston[5] also believed that such damage was a necessary forerunner of abscess formation. Matson and Salam[3] believed that such brain damage does in fact occur, and made the suggestion that if there is increased viscosity of blood in the polycythaemic patient, cerebral anoxia leading to cerebral softening may result. Bacterial infection at such a site of softening could then produce an abscess. Gluck *et al.*[4] held the same view, but neither of these groups of workers believed paradoxical emboli to be responsible. The common sources of emboli are a systemic venous thrombosis and bacterial endocarditis. The authors pointed out that both these conditions are uncommon in the type of patient under consideration. Newton[9] also found little evidence of bacterial endocarditis in the cases of cerebral abscess associated with cyanotic congenital heart disease which he reviewed.

Several authors[5,11-13] have expressed the view that dehydration, from whatever cause, is the factor which increases blood viscosity and so results in vascular occlusion. If there is bacterial infection of such a lesion, an abscess will result. Such infection might follow a minor illness, with organisms reaching the brain by blood which has escaped the pulmonary filter. If there is no infection, the result will be a vascular lesion without suppuration. Martelle and Linde[14] held a different view, namely, that cerebrovascular accidents in these cyanosed children are more likely to result from a relative iron-deficiency anaemia than from the effects of polycythaemia. It is probable that both dehydration and iron-deficiency anaemia are of importance in initiating these vascular lesions. Paradoxical embolus, while possible, is probably a rare cause of cerebral abscess.

While cerebral thrombosis is said to be more commonly of venous than arterial origin,[15] arterial thrombosis does occur in children, perhaps more frequently than is realized, and especially in the carotid arteries.[15,16] These reports concerned patients without heart disease, but Banker[17] had 4 cases of arterial occlusion in children who had associated congenital heart lesions. Our fifth patient is of interest in this regard. The pathogenesis is variable and various causes have been implicated, such as vascular degeneration and local atheromatous plaques in the carotid artery;[15] generalized vasculitis;[18] trauma;[19] and dissecting aneurysms of the carotid artery.[20] Many of these reported cases were, however, unassociated with congenital heart disease.

Diagnosis

(*a*) *Cerebral abscess.* Severe headache, which may have been preceded by a minor febrile illness, is the earliest and most constant symptom. It is often paroxysmal and may be localized to one side if the child is old enough to indicate this. Drowsiness, vomiting, irritability and epileptiform seizures are common and papilloedema is often present. It may be difficult to assess papilloedema in the presence of the engorgement of the ocular fundi which accompanies polycythaemia. Sometimes it is unilateral, on the same side as the abscess.

There are often focal signs such as hemiplegia, and there may be meningeal irritation. Fever, leucocytosis and a raised erythrocyte sedimentation rate occur, but they are not constant features. The blood culture is nearly always sterile. Lumbar puncture, performed with due care, usually shows a raised CSF pressure, and there may be a moderate increase in protein and cells, but again these are sometimes normal. It is exceptional to find any growth on CSF culture.

The special investigations of value in diagnosis are electro-encephalography, air encephalography and arterio-

graphy. Some writers state that the EEG is the most helpful of these procedures.[3,6] Keith *et al.*[6] felt that a cerebral abscess was most unlikely to be present if the EEG was normal. The typical finding is focal high-voltage slow waves over the site of the abscess. An advantage of the procedure is that it causes the patient little discomfort.

Air encephalograms may be very valuable in showing distortion of ventricular shape or position. This was well shown in our second patient. Arteriography is also of use and is fairly frequently undertaken, though Matson and Salam[3] advised against its use as a routine procedure, owing to the risk of precipitating a thrombotic lesion in a polycythaemic patient.

(*b*) *Cerebral thrombosis.* The symptoms and signs are similar to those of abscess except that their onset is usually more abrupt and signs of increased intracranial pressure are less common. The same investigations are used and the EEG shows a diffuse type of slowing of lesser degree than occurs in an abscess. An AEG is mostly unhelpful, but in arterial thrombosis arteriography often gives conclusive evidence, as in our fifth patient. Stevens[15] stressed the value of decreased or absent carotid pulsation in arterial thrombosis, and Wood and Toole,[21] as well as Van Allen *et al.*,[22] recommended the determination of retinal artery pressure by ophthalmodynamometry. Considerable reduction of pressure in one eye as compared with the other suggests occlusion of the carotid artery on that side. Whether the test is practicable in young infants is another matter.

The patient's age is helpful when trying to distinguish between a suppurative and a non-suppurative lesion, since cerebral abscess, in the circumstances under discussion, is virtually unknown under the age of 2 years. In an article by Tyler and Clark[23] it was said to have been described once, but no reference was given. Maronde,[24] it is true, reported a case of cerebral abscess in a child under 2 years who had a congenital heart lesion, but in this case the abscess was secondary to a middle-ear infection. Chronic ear disease is said to be the commonest cause of cerebral abscess in children,[25] but such a cause is not relevant to the present discussion.

For practical purposes, therefore, if there are suggestive symptoms and signs in a child over 2 years with congenital heart disease of the cyanotic type, the possibility of cerebral abscess should be an early consideration. Below this age occlusive vascular disease is the likely diagnosis.

If the evidence points to an abscess there must be no delay in active treatment. Ominous signs are bradycardia and drowsiness, and they demand urgent neurosurgery if the child's life is to be saved. A turbid cerebrospinal fluid may suggest an ordinary pyogenic meningitis, whereas in fact it may have resulted from leakage of the abscess into the subarachnoid space. Once this occurs, death is almost inevitable.

Treatment

(*a*) *Cerebral abscess.* It is only comparatively recently that cerebral abscess associated with cyanotic congenital heart disease has been diagnosed during life, the earlier reports being postmortem studies. Even now, early diagnosis and treatment are essential to prevent permanent neurological damage.

Once the condition is suspected, antibiotics should be given in full dosage, and when the abscess has been located aspiration should be carried out without delay. In some cases one aspiration may be sufficient, in others it may have to be repeated one or more times. Craniotomy and evacuation is recommended by Matson and Salam[3] only if the abscess is encapsulated and superficial. A very large abscess or poor condition of the patient are contra-indications to radical surgery. Injection of a radiopaque dye into the abscess cavity enables progress to be followed by serial radiographs. Local instillation of penicillin and streptomycin is also favoured. In the great majority of cases the abscess is a single one.

(*b*) *Obstructive vascular lesions.* Some authors believe that active treatment in venous thrombosis is of little value, though Taussig[26] has stated that there may be complete recovery if anticoagulants are given within a few hours of the onset of symptoms. Wisoff and Rothballer, in New York,[18] have reviewed reported cases of cerebral arterial thrombosis in children. Four children, the youngest 5 years old, had been treated with anticoagulants and 2 recovered fully. Without such treatment there were 5 full recoveries, 7 had residual paralysis and 8 died. The majority of children who develop obstructive cerebrovascular lesions are under 2 years of age and, in these, anticoagulant therapy may be very difficult to control. Direct surgery has been reported in a very few cases, but the results have not been very impressive. Other suggestions which have been made include hypothermia and the inhalation of 5% carbon dioxide, the latter to improve the cerebral circulation by producing vasodilatation. It is probable that in most cases the child will be seen when it is too late for the above methods to succeed.

The primary aim in these polycythaemic patients should be prevention of thrombosis. Circulatory stasis must be guarded against by ensuring that an adequate fluid intake is provided at all times, especially during hot weather or a febrile illness, so as to prevent dehydration, which may be a precipitating factor in vascular occlusion. The possible danger of relative iron deficiency should also be borne in mind and corrected if present.

Prognosis

Cerebral abscess is undoubtedly a serious condition, and even in recent reports the mortality rate is still high, being over 35% in McGreal's[27] and over 50% in Matson and Salam's[3] series, though it must be remembered that up to 1956 only a small number of recoveries had been reported. It is hoped that with earlier diagnosis and treatment, consequent on the condition being suspected and investigated without delay, better results will be obtained. Even if the abscess is successfully dealt with there is some risk of subsequent focal epilepsy. It is not certain how great this risk is, but Taussig[28] went so far as to recommend anti-epileptic drugs for the rest of the patient's life.

The prognosis after cerebrovascular accidents is not very good. Tyler and Clark in Baltimore[23] reviewed 72 such cases in children. Fourteen died, and in all there was evidence of damage in the distribution of the middle cerebral artery. A definite arterial thrombosis, however,

was found in only 3 cases and in only one was there a venous thrombosis. It is not clear how many of the survivors were thought to have suffered a venous, and how many an arterial, lesion. The great majority of those surviving were under 2 years of age and only 7 recovered fully. The rest were all over 16 years and 4 out of 8 made a complete recovery. Although the last group was too small for the figures to be of much significance, it may be that if such children can be tided over their first few years they may have a better neurological prognosis. The results in Tyler and Clark's older group are in line with the findings of Wisoff and Rothballer,[18] already quoted for arterial thrombosis, also obtained from older children. Mental retardation and convulsions are also reported as sequelae of these non-suppurative lesions.

CONCLUSIONS

If a child with cyanotic heart disease of congenital origin develops neurological symptoms he may have a suppurative or non-suppurative brain lesion. If he is over 2 years old, and shows evidence of focal neurological signs and increased intracranial pressure, cerebral abscess should be the first consideration. On the other hand, an abrupt onset of similar symptoms in an infant under 2 years should suggest an occlusive vascular lesion.

Electro-encephalography usually gives a pattern of localized slow activity over the site of a cerebral abscess. In occlusive vascular lesions a more diffuse abnormality is seen. Air encephalograms may help to localize a space-occupying lesion, such as an abscess. If these investigations are unhelpful, carotid arteriography may show the presence of an arterial thrombosis. While the lesions described are unpleasant complications of cyanotic congenital heart disease, it is fortunate that they do not occur very frequently.

SUMMARY

The case records of 5 children seen in the paediatric wards of Groote Schuur Hospital are presented as examples of neurological complications which may occur in children suffering from cyanotic congenital heart disease.

The probable pathogenesis of such lesions is discussed and their manner of presentation described, in an attempt to show how they may be differentiated. Mention is made of the special investigations that are helpful in this regard.

Current views on treatment are given and a plea is made for the earliest possible diagnosis, so that if a cerebral abscess is present, treatment can be commenced immediately in order that the child may have the best possible chance of neurological recovery from what is a very serious condition.

We wish to thank Prof. F. J. Ford for his advice; Dr. M. Nellen for cardiological help and information regarding the second and fifth patients after discharge from hospital; the Departments of Neurology and Neurosurgery, Groote Schuur Hospital, for help in the diagnosis and treatment of our patients; Mr. B. Todt for the photographs; and Dr. J. G. Burger, Medical Superintendent of Groote Schuur Hospital, for permission to publish.

REFERENCES

1. Abbott, M. E. (1936): *Atlas of Congenital Cardiac Disease*, p. 60. New York: American Heart Association.
2. Tyler, H. R. and Clark, D. B. (1957): Arch. Neurol. Psychiat. (Chic.), **77**, 17
3. Matson, D. D. and Salam, M. (1961): Pediatrics, **27**, 722.
4. Gluck, R., Hall, J. W. and Stevenson, L. D. (1952): *Ibid.*, **9**, 192.
5. Berthrong, M. and Sabiston, D. C. (1951): Bull. Johns Hopk. Hosp., **89**, 384.
6. Keith, J. D., Rowe, R. D. and Vlad, P. (1958): *Heart Disease in Infancy and Childhood*, p. 602. New York: Macmillan.
7. Cohen, M. M. (1960): Neurology, **10**, 452.
8. Ley, E., Obrador, S. and Ley, R. jnr. (1957): J. Neurosurg., **14**, 458.
9. Newton, E. J. (1956): Quart. J. Med., **25**, 201.
10. Groff, R. A. (1934): Arch. Neurol. Psychiat. (Chic.), **31**, 199.
11. Nadas, A. S. (1957): *Pediatric Cardiology*, p. 466. Philadelphia and London: W. B. Saunders
12. Kaplan, S. and Lyon, R. A. (1959): *Nelson's Text Book of Pediatrics*, 7th ed., p 880. Philadelphia and London: W. B. Saunders.
13. Taussig, H. B. (1960): *Congenital Malformations of the Heart*, 2nd ed., vol. 1, p. 173. Cambridge, USA: Harvard University Press.
14. Martelle, R. R. and Linde, L. M. (1961): Amer. J. Dis. Child., **101**, 206.
15. Stevens, H. (1959): Pediatrics, **23**, 699.
16. Cabieses, F. and Saldias, C. (1956): Neurology, **6**, 677.
17. Banker, B. Q. (1959): Trans. Amer. Neurol. Assoc., **84**, 38.
18. Wisoff, H. S. and Rothballer, A. B. (1961): Arch. Neurol., **4**, 258.
19. Frantzen, E., Jacobsen, H. H. and Therkelsen, J. (1961): Neurology, **11**, 695.
20. Wolman, L. (1959): Brain, **82**, 276.
21. Wood, F. A. and Toole, J. F. (1957): J. Amer. Med. Assoc., **165**, 1264.
22. Van Allen, M. W., Blodi, F. C. and Brintnall, E. S. (1958): J. Neurosurg., **15**, 19.
23. Tyler, H. R. and Clark, D. B. (1957): Arch. Neurol. Psychiat. (Chic.), **77**, 483.
24. Maronde, R. F. (1950): Ann. Intern. Med., **33**, 602.
25. Nestadt, A., Lowry, R. B. and Turner, E. (1960): Lancet, **2**, 449.
26. Taussig, H. B. (1960): *Op. cit.*[13], p. 174.
27. McGreal, D. A. (1962): Canad. Med. Assoc. J., **86**, 261.
28. Taussig, H. B. (1960): *Op. cit.*[12] p. 178.