NEUROLOGIC DISEASES IN INFANCY AND CHILDHOOD

Summary of Seminar

By William A. Hawke, M.D., and John S. Prichard, M.D.
Hospital for Sick Children, and the Department of Pediatrics, University of Toronto, Canada

The seminar was conducted in four 3-hour sessions and aimed to cover the more important features of pediatric neurology.

DEVELOPMENT

Dr. Hawke reviewed the normal development of the central nervous system in the infant and child which is so important in the assessment of neurologic disorders in this age group. It was noted that the nervous system was particularly immature and changing rapidly in the first 2 years of life. Development was related to myelination and it was emphasized that this was not a steady process but a pattern of sequences of rapid and slow growth. Motor and sensory development appeared to develop from above and to proceed downward, so that eye-control develops before hand- and leg-control. Development was related to three functioning levels of the central nervous system—the brain stem, the archipallium, and the neopallium. It was observed that the newborn baby functioned at the brain stem level, and to illustrate this an example was given of the hydranencephalic baby which behaves perfectly normally for the first few weeks of life. The archipallium, which includes part of the temporal lobe, the cingulate gyrus and basal ganglia, supervenes on the brain stem and may be considered responsible for the basic emotions and some primitive motor and sensory control. The neopallium, which includes most of the cerebral hemisphere, becomes dominant in primates. Its function is intellectual rather than emotional and is responsible for skills, discrimination and fine movements. The clinical application of these developmental patterns are innumerable but illustrations were given of changes in physical signs in static brain lesions. It was observed that paresis becomes apparent in the upper limb at 5 to 6 months, and in the legs at 10 to 12 months of age. Abnormalities of co-ordination and disorders of athetoid and involuntary movements usually become apparent between 18 and 24 months of age.

NEUROLOGIC EXAMINATION

Dr. Hawke emphasized that repeated examinations, flexible approach, and observation were particularly important in the neurologic examination of the infant and child. A formal adult-like neurologic examination was impossible until later childhood.

Transient infantile reflexes such as the Moro reflex, the palmar-grasp reflex, and tonic neck reflex usually disappear by 3 to 4 months of age. The Moro reflex does not return once it disappears but the palmar-grasp reflex may return if the frontal lobes are damaged. Persistence of the complete tonic neck reflex is associated with damage to the brain. The abdominal reflexes persist in the presence of congenital or neonatal pyramidal lesions. The plantar reflexes may be physiologically upgoing until the age of 2 years.

INVESTIGATIONS

Neurologic investigations were discussed by Dr. Prichard who emphasized that atraumatic tests, such as the electroencephalogram, should always be carried out before potentially dangerous ones, such as a pneumoencephalogram, when the two might give an equal amount of information.
Lumbar Puncture

Well-recognized indications for the procedure were reviewed but it was stated that measurements of pressure were often neglected. A lumbar puncture should not be performed in the presence of raised intracranial pressure, particularly if a brain abscess is suspected or there is evidence of compression of the brain stem. This latter can often be recognized by pupillary abnormalities, slow pulse or irregular respiration. In these circumstances, coning of the brain stem and death may occur 6 to 8 hours after the lumbar puncture.

Roentgenograms of the Skull

These show bony changes, splitting of sutures and intracranial calcification. The indications are innumerable, but they are performed as a routine in the investigation of cases of focal epilepsy.

Pneumoencephalogram

The lumbar pneumoencephalogram was used to demonstrate structural changes of brain. It was noted that the procedure carried a definite risk. The maneuver is carried out under sedation with pentobarbital up to the age of 1 year, and over this age a general anesthetic is desirable. Normally 25 to 35 ml of oxygen gives good ventricular filling. It has been noted frequently that under the age of 12 to 18 months, air tends to collect in considerable quantities over the cerebral cortex and gives the appearance of cortical atrophy, whereas repeat pneumoencephalograms at an older age may show a normal brain.

Ventriculograms

These are performed in the presence of raised intracranial pressure and are surgical procedures.

Myelogram

This is normally performed when a surgical condition is suspected and therefore should be performed by the neurosurgeon.

Subdural Taps

This maneuver is necessary for the diagnosis of subdural collections. Careful surgical technique is required. The puncture is made in the lateral angle of the fontanelle, 1½ inches from the midline. A 20-gauge needle is used and the examination is always bilateral.

Electromyography

This requires skilled interpretation. It is useful for the assessment of peripheral nerve injuries. It is of considerable help in distinguishing between myopathies and neuropathies. It also reflects the myotonic phenomenon.

Electroencephalogram

The electroencephalogram is a record of function not of structure. It was emphasized that it is an empirical test and that there are absolutely no clinically pathognomonic wave forms. Even the organized 3-second spike-and-wave was not always associated with petit mal. It is of great value in the diagnosis and classification of seizures. It is useful as a screening test for intracranial tumors and of localizing value when the tumor is supratentorial. It localizes supratentorial abscesses accurately. The test is useful in following the course of the effects of trauma, encephalitis and encephalopathy. It is of value in the investigation of some psychiatric disturbances, particularly if they are caused by organic disease.

Arteriography

Experience with percutaneous arteriography was reviewed by Dr. Murphy. The technique is difficult to acquire but percutaneous arteriography has been performed successfully in the first few months of life. It is performed under anesthetic and is a safe procedure in the pediatric age group. It is essential for the demonstration of vascular abnormalities. It is useful for the demonstration of space-occupying lesions in the frontal, temporoparietal and cavernous sinus regions.
CONGENITAL ABNORMALITIES

This subject was discussed by Dr. Prichard who commented that the commonest cause of congenital abnormalities in the central nervous system was failure of proper fusion of the neural folds and their coverings. This results in, among other things, spina bifida, hydrocephalus, dermal sinus and diastematomyelia.

Spina bifida occulta is very common and usually requires no treatment. Operation on meningoceles with the skin intact is an elective procedure and should always be delayed as long as reasonably possible. Meningoceles with imperfect skin covering need emergency plastic repair to prevent infection and meningitis. Operation on meningoepiidiocii is usually contraindicated.

Congenital dermal sinus is an important condition which has not been well recognized. It is frequently associated with dermoid cord tumors and recurrent attacks of meningitis. The external manifestation is a dimple or a sinus. If a sinus is present then operative interference should be undertaken.

Congenital hydrocephalus, obstructive or communicating, is a relatively common problem in infancy. Advances in neurosurgery are altering the prognosis very favorably, making early diagnosis and treatment essential.

Diastematomyelia is a condition in which the cord is transfixed by a bony spur which produces a progressive neurologic deficit affecting the legs and often a neurogenic bladder. It was brought out in discussion that the condition is sometimes associated with a hairy nevus or a dimple overlying the abnormality. Diagnosis is confirmed with the aid of a myelogram, and surgery should be undertaken as soon as the condition is diagnosed.

Craniostenoses of various types are not uncommon, and surgical treatment is indicated. The prognosis for intellectual development, vision and appearance is favorable with early treatment but associated congenital cerebral abnormalities are not uncommon.

ENCEPHALITIS

Dr. Hawke first discussed the viral or polioclastic types of encephalitis. In these the gray matter and cells are chiefly affected. It was noted that the St. Louis, the western equine and the eastern equine types of encephalitis all had high incidence in the pediatric age group, particularly infancy. Rabies has assumed some importance with sporadic outbursts due to heavy involvement of the wild animal population.

Treatment of these types of encephalitis is entirely symptomatic. None of the available antibiotics is effective. Passive and active immunization is effective in the management of rabies. The opinion was expressed that cerebral edema is a considerable factor in the initial stages of encephalitis, and that this could be treated with intravenous administration of 50% glucose or 50% sucrose to tide the patient over a dangerous early phase of the disease.

The leucoclastic type of encephalitis is characterized pathologically by perivenous lymphocytic infiltration, edema and demyelination involving chiefly the white matter. It includes the postinfectious encephalitides. It is believed that the balance of the clinical, pathologic and experimental evidence favored an allergic pathogenesis for this group. In the exanthemata the clinical picture, the frequency of the complication and the prognosis varies with the epidemic. It has been observed that if the child does not die in the first week of the illness then he tends to live. The rate and progress of recovery tends to be highly variable. Sequelae occur in about 20% of cases and behavioral deficits are fairly common. The overall mortality is about 5%. Treatment with ACTH or cortisone has proved disappointing. Treatment with gamma-globulin is still inconclusive but may be of value prophylactically. Treatment with typhoid vaccine is probably ineffective.

Subacute encephalitis, commonly known as Dawson's inclusion-body encephalitis or Van Bogaert's leucoencephalitis, is a sharp clinical entity. It commonly affects children and young adults. The course is a matter of months with fatal termination. It is clini-
cally characterized by mental deterioration and convulsions of the myoclonic and akinetic types. The disease progresses through to coma and quadriplegia. Examination of the cerebrospinal fluid (CSF) gives a paretic colloidal gold curve. The electroencephalogram (EEG) shows paroxysms of atypical spike-and-wave pattern which is almost pathognomonic.

LYMPHOCYTIC MENINGITIS

A lymphocytic cellular reaction in the CSF may be caused by a great number of conditions. Tuberculous meningitis is the most important condition to recognize as early treatment is essential for preservation of life. Both groups of encephalitis of viral or allergic origin are usually associated with lymphocytes in the CSF. Other viral infections such as poliomyelitis, choriomeningitis, the coxsackie virus and the "orphan" group of viruses all produce lymphocytic meningitis. Infectious hepatitis and infectious mononucleosis may produce a lymphocytic meningitis.

Neoplastic conditions of the central nervous system occasionally produce either a lymphocytic reaction in the CSF or neoplastic cells which may simulate lymphocytes. Fungal and protozoal conditions involving the central nervous system may also produce a lymphocytic response in the CSF. Recently it has been recognized that leptospiral infections, Weil’s disease, and canicola fever may also produce lymphocytic meningitis.

CONVULSIVE DISORDERS

Dr. Prichard emphasized that convulsive disorders were the commonest neurologic problem in pediatrics. Seizures could be classified into three groups but there was a certain amount of overlap in each. The first is caused by abnormal discharges occurring in the cerebral cortex and may be termed "focal cortical seizures.” They are almost always the result of an organic disturbance at the site of origin, and this disturbance may or may not be progressive. These seizures can usually be recognized on clinical grounds because the first event in the seizure is referable to a point on the cerebral cortex. The electroencephalogram shows a focal disturbance.

The second group are caused by discharges in the reticular substance and central gray matter. They are sometimes termed “centrencephalic” seizures. They are recognized on clinical grounds by the fact that the onset of the seizure occurs simultaneously on both sides of the body and the aura, if any, is a midline phenomenon. They often occur in brains apparently structurally normal. They are sometimes seen in association with congenital cerebral abnormalities or abnormalities sustained in the first 2 or 3 years of life. It is exceedingly rare for them to be caused by any progressive cerebral pathology. The electroencephalogram shows bilaterally synchronous disturbances.

The third group are caused by extracerebral causes such as hypoglycemia, anoxia, uremia, etc. The commonest in children are the simple febrile convulsions which occur characteristically between the ages of 6 months and 4 years. The prognosis in these is good if the seizures are generalized, last less than 30 minutes, occur in a child who hitherto has been apparently normal and in whom there is an adequate cause for the fever. They have a normal interseizure EEG. Probably less than 2% of children presenting in this way have spontaneous seizures in later life. If, however, the seizure is asymmetrical or atypical in other ways or associated with an abnormal electroencephalogram, the chances of epilepsy occurring later are much greater.

The prolonged convulsion may be treated with paraldehyde, 1.5 ml/4.5 kg of body weight intramuscularly, or phenobarbital 3 mg/4.5 kg intramuscularly. Ether may also be used if there is a poor response to phenobarbital and paraldehyde.

Focal and grand mal seizures may be treated initially with phenobarbital. If sufficient control is not achieved then diphenylhydantoin or primidone may be used. Carbonic anhydrase (Diamox®) may be very effective in the treatment of petit
mal, but it is expensive. Trimethadione and methylphenylsuccinimide may also be used. Akinetic seizures are best treated with the drugs suitable for grand mal. Myoclonic seizures are very resistant to treatment but it is worth trying Diamox® or the ketogenic diet.

Surgery is rarely required in epilepsy but may be necessary if focal seizures are uncontrollable with drugs. In experienced hands about 50% cure may be expected, 25% are improved, and 25% unimproved.

Hemispherectomy may be considered for the treatment of seizures associated with hemiparesis, mental retardation and behavioral difficulties. All these factors, including the hemiparesis may, to a certain extent, be improved by the operation.

**GUILLAIN-BARRE SYNDROME**

This condition was discussed by Dr. Hawke. Characteristically, it primarily affects the motor roots symmetrically. It usually follows some antecedent infection and it is believed that it is produced by a neuro-allergic mechanism. In addition to the polynueuritis, it is sometimes associated with cord and cerebellar changes and increased CSF pressure. The Landry-paralysis phenomenon is probably caused by the Guillain-Barré syndrome. The cell count in the CSF is normal or slightly increased whilst the protein is very much increased. The natural history of the condition is usually complete regression of the signs and symptoms. However, there is a 5% mortality associated with respiratory involvement. Very severe cases may be associated with some residual disability. The essential point of treatment is vigorous management of respiratory failure with tracheotomy and the use of a respirator if necessary. Serious cases maintained by intravenous administration of fluids are very liable to electrolyte imbalance with a low concentration of potassium in the blood.

**NEOPLASMS**

Intracranial neoplasms were discussed by Dr. Hawke. It was remarked that 70% of intracranial tumors are glial, 70% are infratentorial, and 70% midline. The peak age of incidence is between 5 and 8 years. Cerebellar tumors which are the commonest tumors in the pediatric age group may present in two ways. The first is due to an involvement of the vermis and characteristically produces ataxia of the trunk with no incoordination of the arms and legs; it is commonly produced by medulloblastoma which is highly malignant and irremovable. The peak age incidence for medulloblastoma is between 3 and 6 years. The second presentation is due to the involvement of the lateral cerebellum, which produces a more peripheral ataxia and incoordination with nystagmus. It is commonly produced by an astrocytoma. This is a relatively benign tumor and the prognosis with surgical removal is very good. The peak age incidence is between 5 and 9 years. It was emphasized that the differential points are not pathognomonic and that all cases with cerebellar signs should be explored.

The ependymoma and the glioma of the brain stem are also important infratentorial tumors. The ependymoma arises in the roof of the fourth ventricle. Pathologically it appears fairly benign but it cannot be shelled out, as it adheres and is difficult to remove without producing damage to vital centers. It frequently contains calcification. Glioma of the brain stem commonly occurs between 6 and 7 years of age and may be either space-occupying in character or infiltrative. Air studies characteristically show a curved aqueduct and the distance from the basisphenoid to the aqueduct is greater than 3.5 cm.

The commonest supratentorial tumor is the craniopharyngioma which is derived from Rathke's pouch. It may be a solid or cystic, and 80% are calcified which is useful diagnostically. It tends to be adherent, therefore difficult to remove. It is usually very slow in its growth and is compatible with survival for some years. It may present as a cause of raised intracranial pressure. It frequently produces defects of the visual fields, pituitary dysfunction or hypothalamic
disturbances. Treatment consists of attempts at removal or drainage of cysts. The course is often slow and the patient may be maintained for a considerable time with help of a palliative neurosurgical procedure and the management of metabolic disturbances.

Astrocytomas, ependymomas and glioblastomas occur in the cerebral hemispheres. The EEG is often valuable in the localization. The prognosis is generally poor. Astrocytomas require wide resection. Ependymoma can occasionally be removed fairly completely. The glioblastoma is very malignant.

Dr. Hawke discussed a series of 40 cases, from the Hospital for Sick Children, Toronto, of intracranial neoplasm under the age of 3 years. At the time of the survey only three patients survived and the poor prognosis for intracranial neoplasms in this age group was emphasized. Early diagnosis was difficult as the tumors tend to grow very large before they produce symptoms.

**SPINAL CORD NEOPLASMS**

These are a fifth as frequent as intracranial neoplasms. The usually present between 2 and 4 years of age. The neoplasms may be gliomata of various types, extramedullary sarcomata, congenital teratoid or dermoid tumors and nonmalignant lipomata. Patients frequently present with a stiff painful back associated with cord signs. There is progression of signs and symptoms. Lumbar puncture reveals a block and a typical Froin's syndrome. Roentgenograms of the vertebral column show widening of the pedicles in the affected region. A myelogram is required for accurate localization. The prognosis is poor compared to adults. One survey indicates that death occurs in 50% of most series, 25% appear to develop recurrences, and only 25% are completely cured by operation.

**BRAIN ABSCESS**

Sixty per cent occur as direct extentions from infection in the middle ear or fractures; 40% occur indirectly from lung abscesses, bronchiectasis or in association with congenital heart disease. Culture from the direct type of abscess is frequently sterile due to use of antibiotics, but the anaerobic streptococcus is not infrequently grown from the indirect type of abscess. They present with general signs of headache, vomiting and malaise and fever. Focal signs with ataxia are important when the cerebellum is involved, and a visual-field defect is quite characteristic of temporal lobe involvement. Papilledema is common and meningeal signs vary but may be marked. The EEG is very useful in localizing supratentorial abscesses. Treatment consists of the use of antibiotics and drainage of the abscess through a burr-hole. Occasionally removal of a fibrous capsule is required.

**BIRTH INJURIES**

These were reviewed by Dr. Prichard. Facial palsy due to direct pressure on the facial nerve usually is total and associated with a good prognosis. Erb's palsy due to a stretching of the fifth and sixth cervical spinal nerve roots requires treatment in an aeroplane splint and the prognosis is fair. Klumpke's palsy due to stretching of the eighth cervical and first thoracic nerve roots produces paralysis of the hand and is associated with a poor prognosis. Phrenic nerve palsies are associated with a good prognosis. Evulsion injuries of the spinal nerve roots have a very poor prognosis.

Cord injuries are produced most frequently by hyperextension in a breech delivery. Stretching of the cord occurs and injuries are most likely to occur in the lower cervical and high thoracic region. A hematomyelia may be produced. The prognosis depends on the severity of the injury, but is essentially very poor. Annular fibrosis of the cord is a late complication. Treatment consists of correcting any bony abnormality and keeping the back immobilized.

Depressed fractures or dents of the skull occurring during delivery have to be lifted in the first 2 or 3 weeks of life.

**SUBDURAL HAEATOMA**

Dr. Prichard stated that these occurred usually as a result of injury to cortical veins as they pierce the dura to enter the sagittal
sinus. Further veins are torn by growth of the hematoma. Three clinical types of subdural hematoma are recognized—the neonatal, the postnatal and the adult type. The neonatal type frequently follows a difficult delivery and presents with bulging of the fontanelle, alteration of consciousness, hypertonia or hypotonia, twitching, respiratory and cardiac irregularities. Focal signs are rare. Subhyaloid and retinal hemorrhages are common. Diagnosis is made by subdural tap and neurosurgical treatment is required as soon as possible. The postnatal or infancy group commonly present between 6 months and 9 months of life. Birth injury is thought to be responsible for 30% of cases and a history of neonatal injury occurs in 20% of cases. Frequently there are no obvious signs, and subdural hematoma may be a cause of failure to thrive, irritability and elevations of temperature. The condition is also associated with scurvy and poor economic status. Anemia and repeated infections are common. More obvious manifestations are convulsions, vomiting, enlargement of the head, a bulging fontanelle and subhyaloid hemorrhages. Diagnosis is confirmed by subdural taps and the treatment is operative. The adult type of subdural hematoma is characterized by headache, drowsiness, paresis and seizures. Arteriography is a useful diagnostic procedure.

Cerebral hemorrhage of the newborn is difficult to differentiate from subdural hematoma and in most instances subdural taps should be performed. Most cases either die within a few days or make a very good recovery.

**SUBARACHNOID HEMORRHAGE**

It was noted that in childhood spontaneous subarachnoid hemorrhage is most likely to be due to an arteriovenous abnormality. The “berry” aneurysm rarely produces a subarachnoid hemorrhage in the pediatric age group. Carotid arteriography is an essential diagnostic procedure in the investigation of these cases. It should be undertaken immediately as the chances of a fatal recurrence in the first 2 weeks is in the region of 50%. If no vascular abnormality is demonstrated the prognosis is quite favorable. It was observed in discussion that subarachnoid or intracranial hemorrhages occurred not infrequently as a result of a blood dyscrasia.

**VENOUS SINUS THROMBOSIS**

This process may be septic or aseptic in origin. The most important aseptic causes are cyanotic congenital heart disease, trauma, marasmus and sickle cell anemia. There may be no symptoms, but if cortical veins are involved, seizures and focal signs or hydrocephalus may result. The commonest cause of septic venous sinus thrombosis in children is middle-ear disease, and chronic mastoiditis is more frequently a cause than acute mastoiditis. The lateral sinus is most frequently involved, and the symptoms and signs depend upon the fate of the thrombus. In many cases it is absorbed or recanalized and may be asymptomatic. If the clot disintegrates, pyemia with fever and rigors may result. If the clot extends to other venous channels, one of a large number of clinical syndromes may result. If the superior sagittal sinus is involved, raised intracranial pressure is usually the only complication. But if it spreads from here to involve superficial cortical veins, seizures and gross signs are apparent. If it spreads forward to involve the inferior and superior petrosal sinuses, it is common to have a sixth nerve palsy on the affected side and possibly some pain in the distribution of the first division of the fifth nerve. If it spreads further forward towards the cavernous sinus, thrombosis and proptosis and external ophthalmpoplegia will be apparent. If it spreads down into the jugular vein, a tender swelling may be palpable in the neck, and pressure from the jugular bulb in the jugular foramen may produce dysfunction of the ninth, tenth and eleventh cranial nerves.

The syndrome of otitic hydrocephalus is caused by a venous thrombosis spreading from the lateral sinus to the superior sagittal sinus. It presents with headache and papilledema. The cerebrospinal fluid is normal.
apart from some increase in pressure, and a ventriculogram shows small ventricles. Raised intracranial pressure may continue for 6 weeks or more but the eventual prognosis is good in most cases. There is some danger of secondary optic atrophy from persistent papilledema and occasionally subtemporal decompression is required. Repeated lumbar punctures are therapeutically useful.

**CEREBRAL PALSY**

This was discussed by Dr. Hawke. It is estimated that there are about 300,000 cases in the United States. About 3 to 4 cases of cerebral palsy occur per year per 100,000 of the population. Roughly 60% are spastic, 25% are athetoid, 8% are ataxic, and 7% have rigidities and tremors. Important prenatal causes of cerebral palsy are rubella, toxemia, dietary insufficiencies, placenta praevia, and possible exposure to x-rays. The paranatal causes are chiefly trauma and anoxia. Postnatal causes are kernicterus, cerebral infection, anoxia and trauma. Genetic or hereditary factors rarely cause cerebral palsy. It is believed that anoxia is an important common factor in the etiology of cerebral palsy. The basal ganglia are particularly sensitive to anoxia.

Early diagnostic features in infancy are the tendency to opisthotonos, an extensor thrust and a convergent strabismus.

It is estimated that about 25% of patients can be helped and require a therapeutic program; 20% are only slightly involved, 15% are severely involved but mentally normal, 40 to 50% are mentally defective and have a poor prognosis. Recurrent convulsions in patients with cerebral palsy tend to lower the functional intelligence quotient. Further problems in association with cerebral palsy are sensory, perceptual and language disturbances. Deafness is quite often associated with kernicterus. The syndrome of the child with brain injury occurs not infrequently in association with cerebral palsy. This consists of distractability, perseveration, inflexibility and emotional reactions when problems are overwhelming. Special schools designed to reduce extraneous factors are required to handle these children.

Estimation of the intelligence of the child with cerebral palsy may be very difficult, and requires an experienced psychologist used to dealing with such children.

The treatment requires a team effort involving many different professional skills, including occupational therapy, physiotherapy, speech therapy and teacher. A good social worker is most important in handling the parents and integrating the program. The orthopedic surgeon is most important in correcting deformities, releasing groups of spastic muscles and supervising the use of appliances. Neurosurgical attack on the basal ganglia may eventually offer some relief for severe athetosis and disorders of movement and rigidity. Chlorpromazine and reserpine have helped particularly in the child with brain injury. Meprobamate and reserpine are thought to reduce the overflow phenomenon in athetosis.

**METABOLIC DISORDERS IN NEUROLOGY**

Dr. Prichard discussed some of the known metabolic disorders affecting the central nervous system and speculated on the role of metabolic research in discovering etiologic factors in various neurologic disorders.

The nervous system is particularly dependent on a normal metabolic state, and is highly sensitive to disorders and deficiencies in metabolism and fluid and electrolyte balance.

Disturbance involving the Kreb's cycle will give rise to peripheral neuritis and possibly encephalopathy. It is reflected in the finding of an elevated concentration of pyruvate in the blood. Not uncommonly this is due to a deficiency of vitamin B$_12$, which is a coenzyme necessary for the oxidation of pyruvate. Administration of the vitamin will cure these patients, but if the concentration of pyruvate remains high it is likely that there is some other disturbance in the Kreb's cycle.
Wilson's disease is due to a genetically determined deficiency of ceruloplasmin. This is associated with increased absorption, deposition and excretion of copper. The concentration of copper is low in the blood. Copper is deposited particularly in the liver, basal ganglia and in the cornea producing the characteristic Kayser-Fleischer ring. Some hope is held out that treatment with dimercaptoprol and interference with the absorption of copper with sulfide preparations might reverse some of the manifestations of the disorder or stop its progression.

Phenylpyruvic oligophrenia is another example of an inborn error of metabolism which is associated with mental retardation and sometimes seizures and an eczematous rash. These children characteristically have fair hair and a fair complexion. The basic disorder is a genetically determined interruption in the metabolism of phenylalanine to tyrosine. The phenylalanine is largely metabolized to phenylpyruvic and phenylactic acids which appear in the urine where they may be detected by the ferric chloride test.

Vitamin B₆ deficiency in infancy is a cause of convulsions and may be detected by the tryptophane-loading test.

It is highly probable that future advances in neurology will be dependent on a biochemical approach.

MUSCULAR DYSTROPHY

This was discussed by Dr. Murphy and defined as a group of heredofamilial disorders of mobility, characterized by progressive weakness and wasting of skeletal muscles. There is no demonstrable disease in the nervous system. The incidence of the main types of muscular dystrophy is 1 in 22,000. Variations are frequent. Classification is important for genetic and prognostic reasons. The main groups are the Duchenne, the facio-scalpohumeral, the limb-girdle, and the myotonic. The characteristic way by which patients with muscular dystrophy arise from the supine position is not pathognomonic but may be observed in the presence of muscle weakness from any cause. The electromyogram and muscle biopsy are most helpful in the diagnosis, and help to distinguish between myopathies and neuropathies, and types of myopathy. It is particularly important to distinguish polymyositis which may resemble muscular dystrophy closely but which may undergo spontaneous remission or respond favourably to ACTH or adrenal steroid therapy. Cases of primary polymyositis with spontaneous remission are probably responsible for so-called cures of muscular dystrophy. There is still no effective treatment for muscular dystrophy. The discovery of two animals, the house mouse and sheep, with inherited myopathies may help considerably in the study of muscular dystrophy.

AMYOTONIA CONGENITA

It was thought that the term amyotonia congenita must be regarded as a syndrome of muscular weakness and hypotonia in infancy rather than a specific entity. The most important type is the Werdnig-Hoffman progressive infantile muscular atrophy which may be manifest before as well as after birth, and which usually has a fairly rapid downhill course with death in infancy or in the first few years of life. There are characteristic changes in the anterior horn cells in the spinal cord and secondarily in the muscles. Progressive muscular dystrophy and polymyositis may manifest themselves in infancy. The term benign congenital hypotonia probably covers Turner's benign myopathy and Krabbe's universal muscular hypoplasia. The babies are weak and flabby, yet there is no paralysis and respiratory movements are normal. Physical landmarks are late but 50% eventually make a complete recovery whilst the other 50% are moderately handicapped. Electrical reactions and muscle biopsies are usually normal in this group.
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