Acute Optic Neuritis

Acute optic neuritis is characterized by the onset of blurred vision, usually in one eye. The visual disturbance usually takes the form of a unilateral central scotoma, which gradually enlarges over a few days, persists for one to three weeks, and then gradually improves. The pupil on the affected side is usually dilated and its contraction to direct light is ill-sustained (Kestenbaum’s sign). \(^1\)\(^2\)

Over 80% of the patients with acute optic neuritis are between 20 and 50 years old, \(^3\) and the condition is twice as common in women as in men. The presenting symptom may be pain or tenderness in the eye, which is made worse by movement of the globe, particularly in a lateral direction. The pain is usually situated in or around the eye, the supraorbital region, or the frontal area, and it persists for several days and occasionally for as long as two or three weeks.

If no abnormality of the optic fundus is seen the condition is called “retrolubar neuritis,” but in nearly a quarter of cases there is some pinkness of the disc with blurring of its margins (“papillitis”). \(^3\) Sometimes the oedema of the disc is so severe that it resembles papilloedema. The oedema may spread to affect the retina and there may even be associated haemorrhages, though these are usually close to the disc margin (“neuroretinitis”).

The differential diagnosis of unilateral central scotoma is sometimes difficult. Retinal vascular occlusion produces a more sudden onset, and the narrowed arteries (if the occlusion is arterial) or congested veins and haemorrhages (if venous

Disorders of Tyrosine Metabolism

During the last decade reports have appeared with increasing frequency describing clinical disorders in children associated with abnormalities of tyrosine metabolism. The reader may easily become confused by them, since there is no general agreement on terminology.

Tyrosinosis (also called hereditary tyrosinaemia, tyrosinæmia, hepato-renal dysfunction) is a disorder first described by K. Sakai and T. Kitagawa in 1957 \(^4\) in a Japanese infant, and subsequently by others. \(^5\)\(^6\) It is inherited probably as an autosomal recessive condition. The syndrome includes cirrhosis of the liver and renal tubular defects, with vitamin-D-resistant rickets, and is associated with a moderate rise in the serum tyrosine up to about 10 mg per 100 ml. (normal up to 3 mg, depending on age and method) and tyrosyluria (which denotes excretion of tyrosine and its metabolites). A number of infants, particularly of French-Canadian origin, have had methioninaemia in addition \(^7\); these infants had a foul smell. The condition is associated with a deficiency of \(p\)-hydroxyphenylpyruvic acid oxidase (\(p\)-H.P.P.A. oxidase) in the liver. \(^8\) The prognosis for untreated patients is poor. In some of them liver failure and death occur within the first 8 months or so of life, particularly if methioninaemia is present. \(^9\) Recent reports \(^10\) on the treatment of the condition by a diet low in tyrosine and phenylalanine, and in methionine too if necessary, are so encouraging that it should always be attempted in a properly diagnosed patient. Adequate facilities for controlling the diet and carrying out laboratory tests are essential.

\(^{1}\) Rose F. C., Postgrad. med. J., 1964, 40, 692.
As early as 1939 S. Z. Levine and his co-workers showed that premature infants fed on a high-protein diet excreted p-hydroxyphenylpyruvic acid and p-hydroxyphenylactic acid in their urine. It is now well known that raised levels of tyrosine in the serum, together with tyrosuria, occur frequently in newborn infants, especially if they are premature (neonatal tyrosinaemia, hyperphenylalaninaemia of premature infants). In a study of 15,000 infants severe tyrosinaemia was detected in 30% of the premature and mild tyrosinaemia in 10% of the full-term infants. This type of tyrosinaemia is more likely to arise when the infant's intake of protein is high, and it usually responds dramatically to a reduction in protein or the addition of ascorbic acid to the diet. In any case it usually clears spontaneously a week or so after birth. It is known that p-H.P.A. oxidase is only minimally active in foetal liver, the activity increasing fivefold at term and thirtyfold in adults. The accumulation of p-H.P.A. itself inactivates the enzyme, which requires the presence of ascorbic acid or other reducing agents to maintain its activity. The serum tyrosine may rise as high as 30 mg per 100 ml, but from a careful study of newborn babies receiving various protein intakes M. E. Avery and colleagues concluded that the condition is generally harmless and that no consistent clinical syndrome is associated with the raised tyrosine level. Since an occasional infant with tyrosinaemia was lethargic, these authors considered that the needs of each infant should be considered individually.

In addition, infants of low birth weight who had tyrosinaemia have been assessed at intervals up to 56 months after birth to determine whether raised tyrosine levels had any long-term effects. No more developmental or neurological abnormalities were found than in infants with normal tyrosine levels. However, it has been suggested that since high intakes of protein are unnecessary, they should be avoided in the feeding of premature infants, who should be given additional ascorbic acid after the first week of life.

Occasionally tyrosinaemia in the newborn may persist for some weeks (transient hyperphenylalaninaemia). Surveys have shown that it occurs in 1 to 1.5% of full-term infants and sometimes may persist for 10 weeks or so, even in babies receiving only a moderate intake of protein. It is not reversed by extra ascorbic acid. In general transient hyperphenylalaninaemia appears to be harmless. Though several reports describe individual patients with various signs and symptoms in association with it, at present it is not clear how they are related.

The differentiation of prolonged transient hyperphenylalaninaemia from tyrosinaemia is not easy in early life. In view of the beneficial effect of diet in true tyrosinosis, P. W. K. Wong and colleagues have suggested that it is logical to employ dietary treatment in cases of doubt and check the need for it periodically by adding protein to the diet. They consider that if abnormalities recur after the age of 10 months a diagnosis of tyrosinosis may justifiably be made.

With the increasing use of screening tests on the blood of infants, in particular for phenylketonuria, patients with neonatal tyrosinaemia and transient tyrosinaemia will be recognized more frequently. It must be emphasized that synthetic diets deficient in essential amino-acids are potentially dangerous and should be given only when tyrosinosis is a real possibility. The patient must be under continuous review, and skilled dietetic advice and careful laboratory control are essential.

### Cholestasis and Cholangitis

Various terms have been used to describe the syndrome comprising jaundice of an obstructive type, itching, pale stools, and dark urine, but in which the main bile ducts outside the liver are patent. One of the commonest is intrahepatic cholestasis. In the Humphry Davy Rolleston lecture published in this issue of the B.M.J. page 515 Professor Sheila Sherlock describes the different diseases which may lead to this type of jaundice as the "chronic cholangitides." The exact site at which the intrahepatic biliary passages are affected varies. She defines the cholangiole as that portion of the intrahepatic biliary tree which extends from the smallest canaliculus between the liver cells to the main sepal bile ducts. It includes the ductule, or canal of Hering, leading from the canaliculus to the interlobular bile duct, which is the first duct to be accompanied by a branch of the portal vein and hepatic artery in the portal tract. The interlobular bile ducts form the sepal bile ducts. These join together to form the right and left main hepatic ducts, which emerge from the liver at the porta hepatis.

In many conditions of cholestasis lesions may be present in both intrahepatic and extrahepatic parts of the biliary tree. This is true for primary and secondary sclerosing cholangitis. In the latter the intrahepatic bile ducts undergo a progressive sclerosis as a result of prolonged extrahepatic obstruction, usually due to gallstones, with infection in the biliary tree. This sclerotic process may explain why jaundice sometimes fails to clear after an apparently successful reconstructive operation on the large ducts. So-called "primary" sclerosing cholangitis may complicate long-standing ulcerative colitis. Radiography shows beading of the intrahepatic bile ducts and...