Treatment was initially by intramuscular and intrathecal kanamycin and chloramphenicol but CSF culture remained intermittently positive for eleven days; therapy was then changed to intramuscular (16 mg/day) and intraventricular gentamicin (2 mg per dose) together with hydrocortisone (10 mg per dose). Only one further positive culture was obtained. The highest CSF polymorph count was 8500/mm^3 in the lumbar theca and 5500/mm^3 in the lateral ventricle. CSF did not become fully normal until much later. The infant developed considerable progressive hydrocephalus. The two lateral ventricles did not communicate, so intraventricular injections were given into each ventricle separately. The Sylvian aqueduct also became blocked. CSF gradually approached normal and all treatment was stopped at 56 days of age.

Pulmonary lesions resolved slowly and the infant was well apart from rapidly increasing head circumference and obvious clinical hydrocephalus. At 3 months of age he weighed 3500 g. He did not follow light and his pupils did not react. His head circumference continued to increase rapidly and at 5 months reached 49 cm, approximately 10 cm above normal for his age and weight. He now followed objects with his eyes.

At this stage his CSF pressure exceeded 300 mm. A pneumoventriculogram showed gross hydrocephalus with bilateral porencephalic cysts, but the lateral ventricles were now communicating. 15 May 1970: ventriculocardiac shunt.

Subsequent progress uneventful. At age 2½ years physical and intellectual development were normal, head circumference 49 cm.

Comment

This infant's prognosis might have been considered hopeless: severe prematurity, respiratory distress syndrome, *E. coli* meningitis and septicæmia pursuing a chronic course leading to hydrocephalus and apparent blindness. Nevertheless intensive antibiotic therapy, including prolonged intrathecal and intraventricular injections, led to recovery from the meningitis; the resulting hydrocephalus was successfully treated with shunt therapy. This resulted in recovery of vision, which is not uncommon in such situations (Lorber 1967). The long-term results indicate complete recovery. In most instances recovery from neonatal meningitis is far easier and more complete if adequate antibiotic treatment is given by the intrathecal as well as by the systemic route, and if diagnosis is not unduly delayed.

[Four other cases of neonatal meningitis due to various organisms were presented, in which the children became fully normal.]

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Colonic Retention Syndrome (Megacolon) Associated with Immaturity of Intestinal Intramural Plexus

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Most of the essential neuromuscular functions of the body, whether they be limb movements, respiratory movements, passage of urine, have already occurred *in utero* before birth. The almost uniform admixture throughout the whole intestine of swallowed squamous epithelial cells within meconium reflects the motility of the bowel throughout its length, but an essential function that does not occur *in utero* is that corresponding to defæcation. In the normal baby the passage of meconium occurs after birth, the stimulus of intrauterine hypoxia to its onset being one of the best known indications of intrauterine distress.

There is a well-recognized group of babies in whom there is a delay in passing meconium, and in whom the terminal parts of the colon and rectum appear to have missed the usual churning up of meconium, resulting in a plug of pale tenacious dehydrated meconium which requires dislodgement by the examining finger.

In the infant the reflexes associated with defæcation are extremely complex and the act of defæcation probably depends upon a series of superimposed reflexes of which we have very little knowledge, particularly from the sensory side.

The best known cause of inability to defæcate is the condition usually known as Hirschsprung's disease, in which the intramural plexus of the rectum and sigmoid are defective in ganglion cells and/or show an overgrowth of nerve trunks. While the diagnosis of classical Hirschsprung's disease seems to be relatively simple and clear on patho-anatomical grounds, it is not an 'all or none' condition and, particularly in the neonatal state, there are many cases that do not fall into the classical grouping.

Causes of the 'colonic retention syndrome' in young infants may be classified as follows:

Nonorganic
Spasm, anal fissure, &c.
Psychological
CNS disease (spina bifida, spastic)

Organic
Aganglionosis, Neuromatosis } classical Hirschsprung's
Immaturity of plexus
Dysplastic
Degenerative – toxic, septic

It is important, surgically, to separate causes that do not appear to be associated with deformities within the muscle and nerves of the intestine, i.e. nonorganic, from those where some intrinsic histological deformity can be found. Our present purpose is to draw attention to a particular group of children in whom inability to defæcate appears to be associated with neuronal immaturity of the intrinsic nervous system of the bowel.

The development of the intramural plexus of the intestine is progressive but not uniform. Neuroblasts can first be found in the foregut at approximately 5–6 weeks gestation. Extension of such areas is progressive throughout the foregut and small intestine so that by 12 weeks, neuroblasts can be identified throughout the whole length of intestine. While most of the development of intramural plexus arises from the foregut, a separate element commences in the region of the cloaca, and there is a concomitant development into the rectum, principally during the second and third trimesters, while the primitive neuroblasts within the small intestine acquire the characteristics of mono- and multi-polar ganglion cells. While quite recognizable neurones are normally visible throughout the myenteric plexus of the whole intestine from about 30 weeks gestation onwards, birth is merely an incident in the maturation and development of the plexus, so that there is an increase in both the number and size of the nerve cells of the plexus, at least for the first five years after birth.

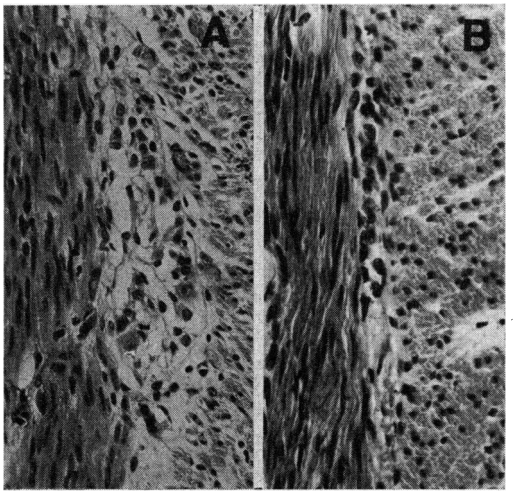

Fig 1 A, *normal myenteric ganglion around time of birth.* B, *showing delayed maturation of neurones.* *H & E.* ×*280*

In a critical survey of 110 children who presented with clinical Hirschsprung's disease at Sheffield Children's Hospital, there were 11 in whom the histological appearance of the anorectal region and colon did not conform to classical Hirschsprung's disease but showed an appearance normally found at 30 weeks or less gestation, i.e. the intramural plexus appeared largely as groups of neuroblasts with very scanty or no recognizable neurones (*see* Fig 1). In a study of 27 children with this condition, Bughaighis & Emery (1971) found that the immaturity of the intestinal plexus extended for a variable distance through the rectum and colon and, in 7 cases, extended to the jejunum. In 3 cases there were isolated zones of plexus immaturity within the bowel, not affecting the rectum, and associated with local functional obstruction.

Only 9 of these 27 children ever passed meconium spontaneously. Fourteen presented with abdominal symptoms within 24 hours of birth, 6 within 48 hours, 4 within 3 days and 2 between 4 and 7 days. A third of the 18 deaths occurred within 48 hours of birth. In 8 children the gestation period at birth was known to be 36 weeks, and in 14 it was known to be over 36 weeks. Eleven of the children initially presented in hospital with respiratory distress syndrome.

The importance of intestinal autonomic immaturity lies in its recognition. Some of our patients died with undiagnosed intestinal obstruction while under observation for respiratory distress syndrome. A child with an immaturity in one system is likely to have an immaturity in another (Dunn 1963).

Our concept of maturity of a child is often a general one but each organ has a histological maturity pattern and the maturity profile of one child is never exactly the same as in another. In a full-term child the maturity of all organs is well beyond any symptom-producing level, but in children of less than full-term maturity, or subject to intrauterine disease, organs may show widely differing patterns of maturity, any or several of which can be of importance to survival.

In our series of 27 children with symptoms produced apparently by intestinal autonomic immaturity, only 9 are still living. The question obviously arises whether an immature plexus is capable of later maturation and whether we are dealing with a more severe form and extension of the well recognized but unexplained condition of meconium plug. This is under study, but our surgeons are at present treating such cases in a conservative and expectant fashion.

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