

ENCEPHALOPATHY FOLLOWING DIPHTHERIA- PERTUSSIS INOCULATION

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Involvement of the nervous system during the course of pertussis was originally described by Trousseau in 1877. It is now appreciated that the injection of pertussis antigen may be attended by a similar effect, and the occurrence of encephalopathy has been reported by various authors including Brody and Sorley (1947), Byers and Moll (1948), Toomey (1949), Anderson and Morris (1950) and Grace (1950).

The fact that the administration of any biological drug entails a certain risk has been glossed over in many textbooks, and the low incidence of complications compared with the number of inoculations performed annually has perhaps diminished appreciation of the hazard.

A case of encephalopathy following inoculation with a mixed diphtheria-pertussis vaccine is now reported.

Case Report

The patient, a girl, aged 11 months, was admitted to hospital on May 3, 1952. Ten days before she had received the last of three immunizing doses of suspended diphtheria-pertussis prophylactic (Glaxo). One millilitre of this vaccine, which contains 20,000 million *H. pertussis*, was given at monthly intervals by deep subcutaneous injection, and had previously been free from untoward effect. Vaccination at the time of the first inoculation had resulted in a typical primary vaccinia.

Three days after the last inoculation the child fell from her pram. Although no serious injury was sustained, she became sick and fretful two days later. During the ensuing few days she became increasingly irritable and listless, and ceased to crawl or stand. The child was apyrexial but it was observed by her doctor that active leg movements were lacking and arm movements were weak. No relevant previous history was obtained; there was no family history of epilepsy or of other cerebral disorder.

Clinical examination disclosed that all limbs were weak and flaccid. The child was unable to sit up, stand, or crawl. The optic fundi presented a normal appearance and there was no evidence of disturbed cranial nerve function. The arm reflexes were feebly present; the knee jerks and ankle jerks were equal but over-active. The

plantar responses were flexor. Otherwise, physical examination disclosed no abnormal features.

When lumbar puncture was performed on May 30 a clear fluid under normal pressure was obtained. There was no evidence of spinal block. Cytology was normal, and the fluid was sterile on culture. Biochemical examination furnished the following results: Glucose, 58 mg./100 ml.; chlorides, 673 mg./100 ml.; protein, 38 mg./100 ml. Pandy's test was weakly positive.

On June 2 there was evidence of bilateral pyramidal tract dysfunction. The plantar responses were extensor, the abdominal reflexes could not be elicited, and the tendon reflexes were grossly over-active, particularly on the right side. Right-sided ankle clonus was elicited.

By June 9 there was some evidence of recovery. Improvement continued, and by July 10 evidence of organic nervous disorder was minimal. A further lumbar puncture on that date yielded a cerebrospinal fluid normal in all respects. On this occasion the protein content was 21 mg./100 ml. and Pandy's test was negative.

Clinical examination on November 18 revealed no evidence of neurological disorder. The child was otherwise well and developing normally.

The history of recent inoculations with anti-diphtheria-pertussis vaccine, the flaccidity and the evidence of pyramidal tract dysfunction, suggested the diagnosis of encephalopathy following prophylactic pertussis inoculation.

Although such complications are by no means confined to pertussis prophylaxis, it is doubtful if generalized reactions of this nature occur after injections of the currently available diphtheria prophylactic vaccine alone.

The history of the fall from her pram suggested initially that this infant might have had a traumatic intracranial lesion such as sub-dural haematoma. Although generally encountered in the first six months of life, this condition may occur later in infancy from injuries to the head resulting from falls when the child attempts to stand or walk (Logue, 1951). In the present case, it is possible that trauma played a subsidiary role.

The possible significance of vaccination performed at the time of the first inoculation also merited

consideration. Post-vaccinal encephalomyelitis is generally encountered between the eleventh and fourteenth day after vaccination (Conybeare, 1951). Thus, the long latent period in the present case rendered this diagnosis unlikely. It was considered, however, that vaccination might have exerted a predisposing influence.

Discussion

The pathogenesis of encephalopathy following anti-pertussis inoculation is uncertain. A constitutional tendency or an individual susceptibility is sometimes postulated. This view is not at variance with the widely held belief that an allergic or pathergic state of the nervous system is responsible. Such a state may be an expression of previous specific or non-specific sensitization. It is also conceivable that injection of an antigen might activate a previously latent neurotropic virus. In the case reported the progressive development and the rapid improvement are compatible with an allergic background.

The clinical manifestations vary greatly. Convulsions with or without fever may occur. Muscular weakness, hypotonia, increased tendon reflexes and extensor plantar responses suggest severe cortical dysfunction. In some instances death may result; in others, recovery is attended by evidence of irreversible pyramidal damage, or the later development of epileptic seizures. Some patients recover completely.

Treatment is symptomatic and hence emphasis must be placed on prophylaxis. In the light of our present knowledge the following precautions are suggested: (1) A family or personal history of any neurological disease such as epilepsy should contraindicate anti-pertussis inoculation. (2) Inoculation should be postponed in a child who is suffering from

any acute illness, who is in the convalescent state of any of the specific infections of childhood, or who has recently been exposed to such an infection. (3) If any untoward symptoms, and particularly convulsions, follow an injection, subsequent inoculations of pertussis antigen are best avoided. (4) Until more is known of the aetiology and pathogenesis of the encephalopathies it is probably advisable not to vaccinate a child during the period of pertussis inoculations. (5) The dosage should not exceed that recommended by the manufacturers.

In conclusion I would emphasize that it is essential to preserve a sense of proportion since, as pointed out by Cockburn (1951), such complications are very rare and are twice as common in children suffering from pertussis itself. The benefits derived from inoculation outweigh the risks involved, but these risks may be minimized by careful assessment of the history and clinical condition of the child with special reference to the points mentioned above.

Summary

A case of encephalopathy following inoculation with a mixed diphtheria-pertussis vaccine is reported.

The pathogenesis and symptomatology are briefly discussed.

Certain precautions in the use of pertussis vaccine are suggested.

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