Safety of poliomyelitis vaccines

During the past 20 years live oral poliomyelitis vaccines have proved to be highly effective and very safe. Paralytic poliomyelitis has almost vanished from countries where a sustained vaccination programme has reached the majority of susceptible young children. Once such a serious disease is brought under control and no longer poses a threat the cost-benefit balance swings and even rare adverse effects of the prophylactic procedure generate serious concern. Occasional cases of paralysis after the use of live vaccine, whether coincidental or attributable, have long been recognised, and in 1969 the World Health Organisation arranged a collaborative study to obtain definitive information about such risks and how they might be reduced, if found to be real.

The results of the 10 year collaborative inquiry were recently published.¹ Thirteen countries took part: nine used only live oral vaccine, two used only inactivated vaccine, and two used both vaccines. All cases of acute spinal paralysis were included, irrespective of immunisation history, if paralysis was typical of poliomyelitis and persisted for more than six weeks or until death within six weeks. Cases were classified as "recipient" when the illness had begun seven to 30 days after vaccination; as "contact or possible contact" when illness had begun seven to 60 days after vaccination in a person with whom the patient had been in contact—or, in the absence of any such contact, if a mass vaccination programme had been in progress seven to 60 days before the onset of illness; and as "no known contact" when the patient had developed paralysis but had no history of contact with the vaccine.

Three countries reported no cases during the 10 years. Six (population 403 million) reported consistently low rates (0.07 per million a year). Of these cases, 43% showed some temporal relation to vaccine (52 in recipients, 70 in contacts or possible contacts), an annual mean of 0.03 vaccine associated cases per million population, giving risks not more than one in 100 million a year for recipients and half that for contacts. For vaccinated children the risk was less than one case per million children receiving vaccine. Almost all type 1 polioviruses isolated had "wild type" strain characteristics, and only four of these were isolated as single viruses from recipients or contacts. In contrast, all type 2 and 3 isolates were "vaccine like," 65% of them isolated from recipients or contacts, several from the central nervous system, indicating that most of these cases in recipients and contacts were vaccine related. Most recipient cases were in young children (the age group being vaccinated). Most contact or possible contact cases were in people aged over 15, many of them parents (presumably not themselves immune) of children receiving primary poliovaccination.

The other four countries had diverse experiences. One, with a high level of immunisation with inactivated vaccine, had two outbreaks (82 cases) not associated with vaccine but confined to religious groups rejecting vaccines. Another, where both types of vaccine were used, had a single case in a child who had received only inactivated vaccine (three doses). The third country experienced a large fall in the number of vaccine associated cases after a change from monovalent to trivalent oral vaccine. In contrast, the fourth country reported a persistently high incidence of vaccine related type 2 and 3 cases until 1979, when only type 1 vaccine was given; reversion

to the previous pattern followed return to the use of trivalent vaccine. Despite passing standard tests, the vaccine used in that country seemed to differ in some way from that used elsewhere.

The general conclusion is that live oral vaccine is one of the safest vaccines in use. Rigorous monitoring of the vaccine and continuous epidemiological surveillance linked to laboratory investigations of suspected cases are still essential to ensure that vaccines remain both effective and safe. The occurrence of cases in parents of vaccinated children shows that, unless they are known to have been previously immunised, these parents should receive vaccine at the same time as their children. The adult population now includes some people too young to have become immune by natural exposure during the prevaccine era yet too old to have been thought to need vaccine against "infantile paralysis" in the early years of the programme. These people are also at risk from exposure to circulating "wild" polioviruses, which may be encountered particularly on holiday in popular countries of sunshine, mediocre hygiene, and low costs. Oral poliovaccine may be no less worth while than typhoid vaccine for these vulnerable adults.

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¹ WHO Consultative Group. The relation between acute persisting spinal paralysis and poliomyelitis vaccine—results of a ten-year enquiry. *Bull WHO* 1982;60:231-42.

Persisting nutritional neuropathy in former war prisoners

Peripheral nerve fibres may undergo regeneration after injury, and hence there is a tendency to think that peripheral nerve diseases will recover if the causative agent is removed. In contrast, fibres in the central nervous system have limited powers of regeneration, and so if they are damaged residual symptoms and signs are expected. Nevertheless, peripheral nerve regeneration over long distances—for example, to the hand after brachial plexus damage—is poor, particularly in adults. The degree of recovery after toxic nerve damage varies with different agents; thus recovery from thalidomide neuropathy was poor. Failure of full recovery may occur when the nerve is damaged in the cell body or proximal axon and thus a long length of axon is abnormal, or because there is concomitant damage to central pathways, which have poor regenerative powers. Degeneration which spreads from the distal end of the fibre is a pattern common to many diseases of nerves. The distribution of damage in different types of neuropathy was investigated by Spencer and Schaumburg, who put forward the concept of central peripheral distal axonopathy.¹ The greatest damage may be to the distal end of axons in the peripheral nervous system, as in acrylamide neuropathy,¹ or to the distal end of axons which terminate in the central nervous system, as in clioquinol toxicity.² Hence there are several reasons why diseases of the peripheral nerves are not always completely reversible.

In wartime, starvation may cause a nutritional neuropathy

which may leave permanent neurological abnormalities. These have been documented in 898 former prisoners of war in the Far East.³ Malnutrition may be associated with several different neurological syndromes, although the exact aetiology remains to be established. Under such circumstances multiple deficiencies are common. Experimentally induced deficiency of a single dietary constituent does not produce exactly the same disease as that associated with malnutrition. Peripheral neuropathy, with or without symptoms such as burning feet, amblyopia, or deafness, was the commonest manifestation of nutritional neuropathy.

The incidence of residual optic atrophy and deafness was surprisingly low (4%), and residual symptomatic peripheral neuropathy was seen in nearly as many (3%), half of whom had persistent "burning feet." Abnormal neurological signs without symptoms were found in a similar number. Although there have been few detailed pathological studies of patients with a history of nutritional neuropathy, extensive degeneration of the distal ends of fibres in the posterior columns has been found.⁴ Thus persistent neuropathy is likely to be due to central distal axonopathy. The degree of peripheral axonopathy has not been assessed.

These former prisoners of war are reaching an age when the common degenerative changes of old age are likely to occur. Probably these will be more severe than in their contemporaries, since their neurological reserve may be less. For example, cervical spondylosis causing damage to posterior column fibres will produce a much greater clinical deficit if a proportion of these fibres have already degenerated. The possibility of previous neuronal damage must be taken into account when seeking the cause of apparently new neurological problems in former prisoners of war.

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¹ Spencer PS, Schaumburg HH. Central-peripheral distal axonopathy—the pathology of dying-back polyneuropathies. *Progress in Neuroopathology* 1977;3:253-95.

² Schaumburg HH, Spencer PS, Krinke G, Thomann P, Hess R. The CNS distal axonopathy in dogs intoxicated with clioquinol. *J Neuropathol Exp Neurol* 1978;37:686a.

³ Gill GV, Bell DR. Persisting nutritional neuropathy amongst former war prisoners. *J Neurol Neurosurg Psychiatry* 1982;45:861-5.

⁴ Victor M. Polyneuropathy due to nutritional deficiency and alcoholism. In: Dyck PJ, Thomas PK, Lambert EH, eds. *Peripheral neuropathy*. Philadelphia: Saunders Co, 1975:1030-66.

Interictal behaviour in temporal lobe epilepsy

Over the years our concepts of the types and frequency of interictal psychopathology associated with epilepsy have changed.^{1,2} In the last century the dominant view was that both the intellect and the personality deteriorated on a genetic basis—a concept influenced by Morel's degeneracy theory of mental disorder.^{2,3} At the turn of the century the concept of the "epileptic personality" gradually gained ascendancy, only to recede with the studies of Lennox⁴ showing that most epileptic patients were normal mentally. These findings have been confirmed by modern epidemiological studies which suggest that only one third of patients

have recognisable interictal psychological disorders,⁵ a prevalence similar to that in patients with other chronic cerebral disorders.⁶

In 1948 Gibbs *et al*⁷ reported that patients with psychomotor seizures had a significantly higher incidence of psychopathology than patients with other types of seizure, and we thus entered the era of "psychomotor peculiarity."¹ This view implies that patients with psychomotor seizures or temporal lobe epilepsy are particularly susceptible to personality or psychiatric disorders of various types. The concept has been fuelled by a wealth of experimental evidence showing the importance of the limbic system and temporal lobes in the emotional and behavioural life of animals⁸ and man. There is also much interest in some of the overlapping psychopathological manifestations of "complex partial seizures" and some psychiatric disorders such as schizophrenia in which the limbic system has also been implicated.⁹

In the last 35 years an enormous and largely conflicting number of publications have accumulated on this subject.^{9,10} With notable exceptions the main proponents of the concept have been psychiatrists, while neurologists have been more sceptical. Stevens¹¹ recently summarised nine controlled studies, including three of her own, using either objective or projective psychological tests or blind psychiatric interviews, which failed to show any increase in psychopathology in patients with temporal lobe epilepsy compared with matched patients with generalised seizures or focal non-limbic epilepsy, or control populations.

The latest entrants to the debate have been Bear and Fedio,¹² who concluded that everyone was using the wrong tools for the task, and devised their own scale of rating behaviour and personality, based on clinical observation. They showed that 27 outpatients with temporal lobe epilepsy had a different personality profile from patients with neurological disease and normal controls (as well as showing differences between right and left sided temporal lobe epilepsy). Recently Bear *et al*¹³ reported that 10 hospital inpatients with temporal lobe epilepsy had a significantly different personality profile from 10 matched patients with generalised or focal non-temporal lobe epilepsy. The former were characterised in particular by circumstantiality, deepened affects, and an interest in religion and philosophy. This study was undertaken in a psychiatric hospital, but surprisingly the authors do not give the psychiatric diagnosis in their epileptic groups, even though they imply that the reasons for admission in two such groups are usually different. Mungas¹⁴ showed that a large percentage of the variation in character traits on the Bear and Fedio rating scale can be accounted for by the presence or absence of psychiatric illness in a neurological clinic. Hermann and Riel¹⁵ compared 14 matched patients with temporal or generalised epilepsy. The former showed important differences only in four of the 18 traits on the Bear and Fedio rating scale—increased sense of personal destiny, dependence, paranoia, and philosophical interest. Some of the trends were in the opposite direction to those predicted. These inconclusive data are illustrative of the conflicting literature on temporal lobe epilepsy and behaviour.

It is surprising to a neurologist that striking differences in personality should be expected to be shown in studies of such relatively small numbers of patients. After all, temporal lobe epilepsy is very common. In a retrospective study of 666 patients with temporal lobe epilepsy recruited from all the departments of a district general hospital 57% were mentally normal and only 6% had severe psychological disorders.¹⁶

What reasons are there for the continuing controversy in this difficult subject? Firstly, the terminology is confusing due