Discussion

Simulated SAH,⁴ hypothalamic stimulation,¹¹ and parenteral administration of catecholamines⁵ in animals produce necrotic myocardial lesions, which may be prevented by severing the cord at C2 level or by administering reserpine or propranolol.⁴ A possible effect of the hypothalamic lesions after a SAH¹² is to produce an abnormal reaction of the autonomic nervous system resulting in persistently high excretion rates of urinary catecholamines.² The close association between the hypothalamus and the autonomic nervous system, coupled with the high correlation between hypothalamic and myocardial lesions after SAH,¹³ points to a catecholamine-linked origin of the myocardial necrosis.

The pathological results of this study should be interpreted in the light of results (unpublished) of a recent survey, which showed that out of 54 patients who died of SAH at the South-east Thames regional neurosurgical unit, 49 had hypothalamic lesions similar to those found in this study and 42 of these patients (78% of the whole) had necrotic myocardial lesions. Thus the fact that in our study all six patients who died in the drug-treated group had "clean hearts" (with normal ECGs) while all six in the placebo-treated group had focal necrotic myocardial lesions (and abnormal ECGs) becomes important. Due to the probable absence of alpha-receptors in the myocardium¹⁴ we presume that propranolol rather than phentolamine was the agent responsible.

What are the clinical implications of these results? Excessive amounts of catecholamines may induce heart failure, as in the cardiomyopathy associated with pheochromocytomas.¹⁵ Some other types of congestive cardiomyopathy may well result from an abnormal interaction between catecholamines and the myocardium and benefit from beta-blockade.¹⁶ A recent report¹⁷ described such a cardiomyopathy, which was cured by stopping treatment with ephedrine. Some authors consider that catecholamines play a crucial part in the onset of myocardial infarction,¹⁸ thus suggesting an explanation for the protective effect of beta-blockade on the ischaemic myocardium. Despite its "cardioprotective effect," propranolol did not influence mortality in cases of SAH and accompanying myocardial damage. This is because lethal secondary events such as a

second SAH are not critically influenced by propranolol or phentolamine, though the results of this preliminary study suggest a possible protective action of these two drugs with regard to cerebrovascular spasm. In other "stress areas" with associated myocardial necrotic lesions and unstable cardiac rhythms, such as head injuries,⁷ beta-blockade may have an important role. The source of hearts for cardiac transplantation is another important, though perhaps more remote, factor to be considered. If, as is often the case, the donor has died after a cerebrovascular accident or head injury then early administration of a beta-blocker to the potential donor might be wise.

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Requests for reprints should be addressed to G Neil-Dwyer.

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National Childhood Encephalopathy Study: an interim report

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Summary and conclusions

Data from the first year of the National Childhood Encephalopathy Study were reviewed to see whether any relation was apparent between pertussis vaccination and brain disease. Three hundred and eighty-seven cases of encephalitis and other specified neurological

conditions in which the children were admitted to hospital were reported, of which 267 satisfied the study criteria. Control children were matched for age with the index cases, and medical and immunisation histories were reviewed. Few of the index cases had been vaccinated within 28 days before admission to hospital, so that no close association between vaccination and brain disease existed in most cases.

The number of children who had recently been immunised was too small for any statistically useful conclusion to be reached about the risk associated with pertussis vaccine. The study is continuing.

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Introduction

Allegations that immunisation against pertussis carries a risk of causing permanent brain damage in an appreciable

number of children^{1 2} have prompted much public concern, and immunisation rates have declined.^{3 4} Most published evidence supporting this suggestion rests on series of case studies without equivalent data on controls and is subject to conflicting interpretations. The National Childhood Encephalopathy Study (NCES) was set up in 1976 to help meet the urgent need for more adequate evidence.

It is usually wise to refrain from publishing results of a scientific study that has not ended unless they are unexpected and have grave implications. It would be imprudent to depart from this general rule in the case of the NCES, particularly in view of the far-reaching consequences of any conclusions that might be reached. Because of the degree of concern that has been expressed, both among doctors and by the public, over the alleged dangers of pertussis vaccination, however, we consider it to be appropriate to indicate progress based on the first year's data.

Study method

We ask paediatricians, infectious-disease physicians, and neurosurgeons throughout England, Scotland, and Wales to notify cases of encephalitis and certain other specified neurological conditions in children aged 2 months to 3 years admitted to hospital under their care. A standardised postal inquiry about clinical findings and outcome is made in each case. Children who have not recovered within 15 days after admission are visited and examined by a paediatrician on the study team at intervals over at least 12 months. Two controls matched for age are selected from the population of the same health authority area as each index case. For children with persistent neurological defects two additional controls are selected from among children admitted to the same hospital.

Community physicians and general practitioners are asked to provide immunisation histories for cases and controls, and in both groups the mother is interviewed at home to ascertain factors in the medical histories of the child and the family and in the social environment that might predispose to serious neurological illnesses.

Progress

During the first year 580 hospital consultants and their teams co-operated in the study; 387 cases were reported, and 267 satisfied the study criteria. Almost half the children (45%) still had neurological symptoms or signs 15 days after admission to hospital. The modal age of this group was 5-6 months. Since primary immunisation usually starts at about this age, the chances of a coincidental association between vaccination and onset of encephalopathy are then inevitably at their peak.

Past history—About one-third of the children with persistent neurological defects and two-thirds of those who recovered had a

history of an acute infectious disease current at admission or within the previous four weeks. Most were illnesses commonly associated with high fever, which may trigger prolonged convulsions. Some children had a history of neurological problems in their first four weeks, retarded development, or previous convulsions. Such conditions are included in the contraindications to immunisation given by the Joint Committee on Vaccination and Immunisation.⁵ This advice is based on the prevalence of such histories in children who develop acute encephalopathic illnesses and on the fear that vaccination may rightly or wrongly be seen as a precipitating factor and blamed for any ensuing damage.

Diagnosis—Forty-two per cent of the children had convulsions lasting over 30 minutes; encephalitis was diagnosed in 26% and infantile spasms in 15%. The remaining children had various other conditions.

Immunisation—The history of immunisations within 28 days before admission to hospital for index children and within 28 days before the day on which they attained the same age for control children was examined. Most of the index children were not vaccinated within this interval, and therefore no close association with their brain disease was possible. Too few index cases and controls had been recently immunised to reach any statistically useful conclusion concerning any possible risk associated with pertussis vaccine.

Further plans

In order to study a larger sample of children we are requesting reports on new cases until 30 June 1979, by which time over 1000 cases should have been included. Children with persistent neurological defects will continue to be followed up for at least 12 months after their first hospital admission—that is, until June 1980.

The National Childhood Encephalopathy Study research team wishes to thank all those who have regularly reported cases and responded to requests for information. The success of the study has depended on their painstaking collaboration. We also thank the many parents who have kindly co-operated with our inquiries.

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ONE HUNDRED YEARS AGO A young friend who had been amusing himself with mesmerism, had brought a young girl, in a family in which he was intimate, into such a state of susceptibility, that she would go off into a comatose sleep on his simply pulling her hair. In this condition, she exhibited a number of its curious phenomena, which he was often called upon to demonstrate. On going one evening to a small party at the house of this family, he was introduced to a lady whom he had not previously seen; and he had not been in the room many minutes when, to his own surprise and that of every one else, this lady fell down in a dead sleep, from which she was with difficulty aroused. He was himself at the other side of the room at the time, and was engaged in conversation, without the least thought of the stranger. Having become possessed with my own views of the potent influence of "expectancy" in the production of these phenomena, he determined to trace out its *modus operandi* in this particular case; and learned that this lady had been specially invited to meet him, and had been assured by one of the young ladies of the family, while laying aside her bonnet and cloak in another room, that "Mr S is such an extraordinarily powerful mesmeriser,

that he can send you to sleep by merely looking at you!" Now, as a great deal of hysteric and hypochondriac disorder undoubtedly depends upon the patient's habitual direction of the attention to the part or organ which is the subject of them, so does a great deal of the success of remedial measures, in certain classes of cases, depend upon the patient's expectation of their favourable result. That the "charming away" of warts, for example, is a reality, I have not the slightest doubt; and the different "charms" have this in common, that they tend to fix the patient's attention on the part with the expectation of a cure; the success being generally proportional to the patient's assurance of it. That in persons of emotional temperament the "strong assurance of faith," which is producible by religious influences, has a peculiar potency, is the concurrent result of all experience in present and past times. But the like occurs with impressible subjects, under the influence of a belief in the occult powers of some new physical agency. Thus there can be no doubt that the discoveries of Galvani and Volta, not long previously, prepared the public mind of Paris for Mesmer's doctrine of the magnetic fluid and its professedly curative results. (*British Medical Journal*, 1878.)