Vaccination against Whooping-cough

SIR,—The recent report by the Public Health Laboratory Service (P.H.L.S.) Whooping-Cough Committee and Working Party on "The Efficacy of Whooping-cough Vaccines used in the United Kingdom before 1968" (8 November, p. 329) suggests that the pertussis vaccines used in the U.K. are not very effective in protecting against whooping-cough. The conclusion is based on a study of children, the majority of whom were vaccinated five or more years ago, and are in marked contrast to those obtained by the Medical Research Council investigations[1-3] which studied the protection given by vaccines produced in 1948 to 1952. It is important therefore to inquire into the possible reasons for the apparent failure of the particular pertussis vaccines used in the 33 areas investigated by the Public Health Laboratory Service.

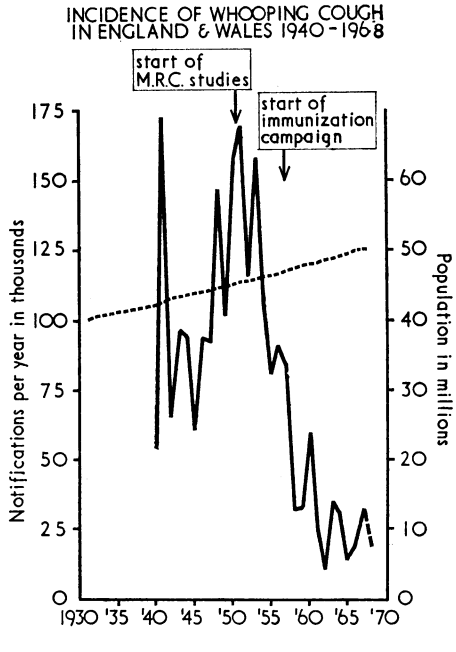
There are a number of factors that have a bearing upon the efficacy of a vaccine. These are: (1) Potency of vaccine; (2) immunization schedules; and (3) proportion of the child population receiving vaccine.

(1) *Potency of vaccine.*—The Medical Research Council investigations already referred to showed that there was a correlation between the ability of a pertussis vaccine to protect mice against an intracerebral challenge with *Bord. pertussis* and the ability of the vaccine to protect children against whooping-cough. Accordingly the mouse protection test was adopted internationally as a means of assessing the potency of pertussis vaccines, and in 1957 a British Reference Vaccine was established for the purposes of checking the potency of vaccines as measured by the mouse protection test. This Reference Vaccine was known to give protection in about 80% of children exposed to the disease in the home.[4] It was not until 1964, however, that the World Health Organization formulated requirements for pertussis vaccine[5] and required that a single human dose of vaccine should have a potency of not less than four international units. With the establishment of an international standard it was subsequently shown that the British Reference Vaccine contained 2·1 international units per single human dose, and it thus became apparent that the British potency requirements were lower than those required internationally. Some vaccines marketed in this country have always had a potency in excess of four units, but many did little more than pass the required lower limit.

The British manufacturers in collaboration with the control laboratory at Hampstead were quick to correct this discrepancy between the British and international requirements, and since 1966 only those vaccines with a potency of four units or more have been marketed. It should be appreciated that the P.H.L.S. study terminated in October 1967 and thus the latest vaccines to be used will have been marketed in or before 1966. Such vaccines will certainly have been made, as bulk components, before 1966, and thus the poorer vaccines giving rise to the P.H.L.S. findings are unlikely to have had a potency as high as 4 i.u./human dose.

A second modification in the formulation of some pertussis vaccines has been made since 1966, which particularly concerns toxicity. It has been shown[6] that a triple vaccine (diphtheria, tetanus, and pertussis) containing an aluminium adjuvant when given by deep intramuscular injection, gives rise to fewer local and systemic reactions than vaccine made from the same components but without the addition of the adjuvant. Manufacturers in this country have confirmed these findings[7] and adjuvanted vaccine is now being made available. Although the adjuvant is added to decrease reactions there is some evidence that it also slightly increases the potency of the pertussis component. On the other hand, there are some vaccines on the market with such high potency that the addition of an adjuvant does not improve the vaccine. Both these modifications, however, are steps in the right direction and should lead to the availability of vaccines which are more effective than those shown to have marginal potency available some years ago.

A third factor which may have played a part was the finding by Preston[8] that the organisms causing whooping-cough today are serotypes



1:3. It must be emphasized that there are no laboratory tests available to guide manufacturers in the selection of suitable strains of *Bord. pertussis* for inclusion in vaccines; the only criteria are that freshly isolated strains agglutinated by pertussis antiserum should be used. After Preston put forward his hypothesis that vaccines should contain organisms of the 1:3 serotype it was found that the manufacturer whose vaccine is of particular concern in the P.H.L.S. study did not contain serotype 1:3 strains. The significance of the inclusion of these strains is not fully understood, but in spite of this they have been a component of all vaccines marketed in Britain since 1966.

(2) *Immunization schedules.*—Over the last ten years there has been a tendency to complete pertussis immunization of infants within the first six months of life since the majority of deaths caused by pertussis occur in the first year of life. More recent work[9] has shown, however, that a better antibody response is obtained when immunization is delayed until the child is 6 months old, and when the period between the first and second dose is 6 to 8 weeks and the third dose is delayed until 6 to 8 months after the second dose. This advice has now been incorporated into the latest schedule of vaccination and immunization procedures from the Department of Health and Social Security,[10] and a much greater efficacy of vaccines may be anticipated from the general acceptance of these schedules which were not in use during the period of the P.H.L.S. study.

(3) *The proportion of the child population immunized.*—It is not known what proportion of the susceptible population must be vaccinated in order to eliminate whooping-cough. It is logical to assume, however, that the greater the proportion of the child population immunized the less susceptible the community will become, and furthermore in such a community the non-immunized individual will be in less frequent contact with the disease. It is interesting to note in this regard that in the P.H.L.S. study about half the cases occurred in Manchester, the population of which is less than one-tenth of the population of the remaining areas, and it may be significant that the number of children immunized against diphtheria, tetanus, and pertussis in Manchester is not as high as in the other areas in the study. Since about half the cases have come from one area then the apparent poor quality of the vaccine used in that area must play a significant part in the conclusions of this study. For this reason alone it would be somewhat misleading to consider that the findings of this report apply in general to the United Kingdom.

It is important that the P.H.L.S. data are put in perspective. The Graph shows the incidence of pertussis in England and Wales from 1940, when the disease was first notifiable, until 1968. Although the M.R.C. trials established the efficacy of pertussis vaccine in 1951 it was not until 1956 that an immunization campaign gathered momentum. It is difficult to account for the marked fall in morbidity after this date for any reason other than successful vaccination, and it would be even more difficult to account for this trend if the vaccines used were less than 24% protective as suggested by the P.H.L.S. study. It is true that in 1967 the notifications of whooping-cough increased as they did in 1952, 1956, 1960, and 1963, but throughout this period there was a general fall in morbidity. Indeed, the notifications from 1 January to mid-October for 1967, 1968, and 1969 are 25,533, 14,556, and 3,888 respectively and we now have the lowest incidence of whooping-cough on record. The P.H.L.S. report informs us, however, that "notifications increased appreciably in 1963 and since then have not declined consistently."

The P.H.L.S. study has, however, served as a warning, and increased efforts should be made to eliminate this disease. It would be little short of a tragedy if the findings were used as an excuse to stop immunization against whooping-cough. The findings of the study relate only to vaccine made predominantly by one manufacturer, available more than five years ago, and used in a schedule now known to be less efficient than those proposed today. Furthermore, the data are collected mainly from a single area which was not extensively vaccinated. Today, there are more potent vaccines available, some of which contain an adjuvant. These improvements, together with the introduction of a more efficient schedule and greater use of the vaccine, should lead to a lower incidence of the disease.

It is important that surveillance of currently available vaccines should continue to

see whether the improvements made by the manufacturers have had the desired effect. It will be more meaningful, however, to take into consideration the outcome of exposure to the disease of all vaccinated children, rather than select the data on which any further analysis is made. Further reports from the P.H.L.S. studies now in progress should prove interesting.—I am, etc.,

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Acetate and Bacteria

SIR,—The significance of the finding of the adverse effect of acetate on bacteria goes far beyond its importance in dialysis solutions (27 September, p. 749). The proved effect of acetic acid on *Pseudomonas* seems to have been largely ignored in surgery.

In Botswana last year we began dressing our burns with vinegar from the kitchen (diluted for comfort), whenever the dreaded green pus appeared. Not only did the green pus rapidly disappear but grafting could be done earlier, and with a much greater success rate. Perhaps those whose patients, wards, and vision are darkened by silver nitrate might give acetic acid another try.—I am, etc.,

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Saving the Grossly Disabled

SIR,—Your leading article (13 September, p. 607) raises an extremely important issue. It would seem that Dr. J. S. Lawson[1] had answered three of the four questions he raised; his studies showed that most parents of children with deformities such as spina bifida prefer a doctor to make a decision whether life-saving measures should be instituted. There remains his first and most important question—should life-saving measures be instituted?

If life-saving measures are carried out the surgeon should bear in mind it is the long-term well-being of both parents and child, not merely for the first 10 or even 20 years of the child's existence, which is the critical point at issue. It is wrong to operate indiscriminately on all cases, ignoring the problem of the subsequent disability to the patient and to the community at large. Surgeons should be moving to a situation in which the indications for a life-saving operation at birth are cut and dried. In some cases where the prognosis is poor it can only be considered a matter of unwarranted meddlesome medicine to intervene actively with surgery and antibiotics.

A particular group in which operative indications should be very carefully considered are children with spina bifida; the number of such children has grown very fast since immediate operation increased the survival rate, and now totals at least 8,000, a great many of whom are severely disabled. I know it is not easy to predict at birth which children will do well, but there is evidence to suggest that the presence of neurological signs, such as partial or complete paralysis of the legs, is indicative of a poor prognosis.[2] A controlled trial of conservative versus immediate surgery took place as long ago as 1962,[3] so we should be in a position to know something of the long-term prognosis of immediate surgery, and which signs at birth have turned out to be of significance; in particular, how many children are paraplegic and incontinent, and whether the I.Q. of children treated with immediate surgery is better than that of the survivors of conservative treatment, at least one-third of whom are mentally subnormal.[4]—I am, etc.,

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Purpura and Ibuprofen

SIR,—I wish to draw attention to a possible association between ibuprofen (Brufen) and purpura. A 33-year-old woman with no known haemorrhagic tendency developed bruises on her upper and lower limbs during the third week of a course of ibuprofen therapy for a painful hip. The normal dose of the drug—namely, 600 mg. per day—was being taken. No other drugs were being given. On discontinuing therapy the rash spontaneously disappeared. Haematological investigation performed a few days after the disappearance of the purpura proved negative. I am unaware of any other report of the possibility of such an association.—I am, etc.,

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Career Prospects for Medically Qualified Dentists

SIR,—Mr. A. L. Gwynne (11 October, p. 113) mentions that the possession of a medical qualification is a great asset in obtaining a consultant post. In some areas this is certainly true, but in others where there is a predominance of non-medically qualified members on the selection board the opposite can be the case.

His letter may have conveyed the impression that the medical qualification was useful only to obtain an appointment, but he can be assured that the consultant dental surgeon derives as much day-to-day usefulness from his medical training as he does from his dental training. Such a statement may seem strange to many readers of the *B.M.J.*, who assume from the title that a consultant dental surgeon does, in hospital, the same as a dental surgeon in practice, and cannot understand why there should be any question of a medical qualification being necessary. In fact, however, consultant dental surgeons have full clinical charge of patients admitted to hospital suffering from severe maxillo-facial injuries, or needing resections of jaw for disproportion or tumours, for skin and bone grafts to the mouth, and for the removal of ectopic teeth. These operations are, of course, performed by consultant dental surgeons because they are better equipped by the dual training to deal with such problems than the person with a surgical training only.

Planning and correlation of careers are difficult to arrange without interfering with personal choice, and although the figures look disturbing at the moment some solution usually appears to sort out the mathematical gloominess of such forecasts. The Hospital Dental Service can take heart that many young people are taking the trouble to train adequately to care for its patients. It is of no importance whether they consider that they are practising medicine with a dental qualification, or dentistry with a medical qualification. They are putting at the disposal of their patients the results of the longest and hardest training in the medical field—a fact which may not be appreciated.—I am, etc.,

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Agricultural Accidents

SIR,—I greatly enjoyed Dr. D. K. C. Cooper's informative article on agricultural accidents (25 October, p. 193), but in the interest of accuracy would take issue with him on one point. In his final paragraph he says that "Legislation alone, however, cannot prevent accidents, and the final responsibility lies with the farm worker to ensure that all safety precautions are followed. . . ." The employer has a very definite responsibility in this field, and the recent Employers Liability (Defective Equipment) Act must be relevant in the 50% of accidents in which farm machinery and implements were implicated.—I am, etc.,

Ewell, Surrey. R. McL. ARCHIBALD.

Fibrinolytic Enzyme System

SIR,—Dr. J. D. Cash and others (4 October, p. 50) suggest that the discrepancy between their results and ours (19 July, p. 137) with regard to the level of fibrin degradation products (F.D.P.) (Burroughs Wellcome) during pregnancy may be due to the presence of residual non-specific sheep-red-cell haemagglutinin in the test serum. In our study negative controls were included by incubating each test serum with the sensitized cells, and any specimens showing non-specific agglutination were either excluded or reabsorbed to remove any non-specific sheep-red-cell haemagglutinins. However, in a