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Non-specific "non-effects" of vaccination

Literature does not support either beneficial or detrimental effects

Papers 1309

This issue carries a paper from Burkina Faso on the non-specific effects of vaccination on survival in children (p1309).[1] The study analyses mortality in a cohort of children as a function of their vaccination status. The authors conclude that vaccination with diphtheria, tetanus, and pertussis (DTP) vaccine as well as BCG is associated with better survival of children up to 2 years of age." The paper should be viewed with caution and in context.

Non-specific effects of vaccination, beneficial or detrimental, have been discussed for about 15 years. Some vaccines have effects on non-target diseases—for example, BCG protects against leprosy.[2] Some vaccines have rare adverse reactions—for example, myopericarditis following smallpox vaccine.[3] High titre measles vaccines were evaluated in the 1980s and withdrawn because of a hint of unexpected mortality in vaccinated girls.[4] This observation stemmed from work by Aaby et al and led to a series of publications linking morbidity and mortality patterns to vaccination in several populations, particularly in West Africa. BCG and standard titre measles vaccines were claimed to be more beneficial than could be explained by their effects on tuberculosis or measles alone.[5 6] Associations found in one population were not always upheld in other populations.[7] Hypotheses shifted, and the higher mortality once attributed to high titre measles vaccines was later attributed to alterations in the DTP schedule.[8] In 2000, the *BMJ* published a paper based on data from Guinea-Bissau, which claimed that diphtheria, tetanus, pertussis, and polio vaccines were associated with higher infant mortality.[9] That report encouraged a series of studies, of which the paper by Vaugelade et al in this issue is one. An independent WHO task force also reviewed all the data and concluded that the finding from Guinea-Bissau relating to DPT was not convincing.[10]

The problem with literature on this subject has been the reliance on observational studies comparing non-comparable populations—non-comparable because vaccinated individuals are different in all populations and in many ways from those who are not vaccinated.[11]

The paper by Vaugelade et al illustrates this problem well.[1] The data on vaccination were transcribed from individual health cards of the children in the context of a demographic surveillance system. Vaccination coverage was low—55% had apparently received no vaccines at all by 6 months of age, and 24% were totally unvaccinated at 2 years. Confounding is obvious, as vaccination was associated strongly with high maternal age, modern obstetric delivery, and presence of a dispensary in the village (such associations are expected). The authors assumed that absence of a vaccination record meant no vaccination. They also say that when a child died, the mother usually discarded its belongings, including vaccination details. Selective misclassification could therefore have occurred—towards unvaccinated status in children who died. The proportion of infants who had cards at successive visits and consistency of data from one visit to the next are not discussed in the paper. People with experience of such data will know how problematic they are. Diarrhoea, fever, and cough in infancy were all associated significantly with vaccination (table 2 in the paper[1]). As it is unlikely that the vaccines caused this morbidity, it probably means that sick children were brought to the clinic and hence selectively vaccinated, and lost cards may have been replaced when ill children visited health centres.

The mortality analyses adjusted for potential confounders on which data were available, but the study was not designed for this purpose and there were no data on factors such as parental education, occupation, or economic status. The conclusion that lower mortality was associated with both the BCG vaccine and the DTP vaccine may be technically correct, but this may be misleading in conjunction with the word effect in the title of the paper. Critical readers will interpret the greatly lower mortality (by 50-75 %) as largely if not entirely a reflection of uncontrolled socioeconomic advantages of the children receiving the vaccines.

The only conclusion justified by this study is that analysis of very problematic data showed no evidence for a positive association between any vaccine and increased mortality in infants. That in itself is reassuring; but it is a long way from saying that the vaccines have non-specific beneficial or detrimental effects. This criticism may be directed at much of the literature on this subject.[5–10]

Are hypotheses of non-specific effects of vaccines tenable or can we study them at all? One problem is that the hypotheses have kept changing, from one to another subgroup effect on mortality, allergic disease, immune response, Gulf war syndrome, or to qualifications that they may be important only in populations subject to a major challenge from infectious disease. Hypotheses are cheap to manufacture but difficult to test, given the non-random allocation of vaccines in routine programmes. Evidence shows that vaccination with some antigens (for example, BCG) can influence responses to other antigens (for example, hepatitis B),[12] but we have no

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convincing evidence that this has any implications for subsequent morbidity let alone mortality.

If we had serious concern over such effects, the best way to evaluate them would be by large cluster randomised trials of different vaccine formulations, or of standard vaccines given according to different schedules. We could contemplate such trials for reasons of overall direct as well as indirect effects. The standard vaccines change over time, and the most widely used timetable (BCG/oral polio vaccine at birth, DTP/OPV at 6, 10, and 14 weeks of age, measles after 9 months) was set 30 years ago at the start of the World Health Organization's expanded programme on immunisation as an optimal compromise considering the vaccines then in use, the disease risks then prevailing, and logistic considerations concerning paediatric clinic policies for children of that era. But much has changed—new vaccines and vaccine formulations, lowered disease risks (largely due to widespread vaccination), and changed child health regimens, which now include micronutrients in many countries. We may need to reconsider the optimal basic schedule for delivery of vaccines and other services to the world's children, and we need to evaluate them if possible with trials—not with observational studies with biased data.

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Competing interests: PF has attended several conferences on vaccines, which were subsidised by manufacturers of vaccines.

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Suicide pacts and the internet

Complete strangers may make cyberspace pacts

The recent deaths of nine people in Japan, in October 2004, apparently in two suicide pacts[1]—seven suicides in one pact and two in the other—have brought the relatively rare phenomenon of suicide pacts into the limelight. What is unusual is that these pacts seem to have been arranged between strangers who met over the internet and planned the tragedy via special suicide websites. This is in contrast to traditional suicide pacts, in which the victims are people with close relationships.

A suicide pact is an agreement between two or more people to commit suicide together at a given place and time. In England and Wales, for epidemiological purposes, people who have committed suicide within three days of each other in the same registration subdistrict are considered potential victims of a suicide pact.[2] A related phenomenon is homicide-suicide, in which a person commits a murder and then ends his or her own life. Dyadic death is a term that encompasses both suicide pacts and homicide-suicides.[3] A suicide cluster is a group of suicides that occur closer together in time and space than would normally be expected in a given community, with suicides occurring later in the cluster being motivated by earlier suicides. In mass suicide, several people commit suicide usually influenced by charismatic leadership, strong loyalties, or religious beliefs.

Two major epidemiological studies on suicide pacts have been carried out in England and Wales, 36 years apart.[2 4] The second study showed that the incidence of suicide pacts had declined by 27% in that period.[2] On average, one suicide pact occurs every month. Suicide pacts almost always involve people well known to each other, mostly spouses, most of them childless. Most of the victims belong to social classes I, II, and III, and a noteworthy proportion work in professions allied to medicine. The methods used are generally less violent; poisoning by exhaust fumes from a vehicle is the most common. But where access to violent means is easier, such as firearms in the United States, suicide pacts entail more violent methods.[5] Most victims leave jointly signed suicide notes.

Although, by definition, both victims make a joint decision to die in a suicide pact, studies of survivors of pacts have shown that this is not always the case.[6] In cases where the decision was not mutual, the deceased member is likely to have been the instigator, male, depressed, and to have had a history of self harm, whereas the survivor is likely to be the coerced, female, not mentally ill, and with no previous history of self harm.

Suicide pacts account for less than 1% of the total number of suicides.[2 4] Both members typically employ the same method. Occasionally, the partners may both use multiple methods to ensure death.[7] About

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