International health at home: Learning from low-income countries

– secondary publication

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ABSTRACT

International health research conducted under extreme conditions in low-income countries may question assumptions which are also important in high-income countries. Examples are given of how observations in Guinea-Bissau have led to reinterpretation of the decline in measles mortality in the industrialised countries, the polio model and the impact of stopping vaccintions after eradication.

INTROCUCTION

International health and development aid have followed a long tradition of charity to reduce the plight of poor people. This unfortunately affects research in international health. Charity does not prioritise research. Research might indicate that we do not know what is best. Only operational research is given priority. Many would consider health research unethical, except in new problems like HIV and resistant TB and malaria; the real problem is to apply our current knowledge to the benefit of the poor.

However, we may not know what is best. There is a need for research which measures the real effects of our interventions and questions our basic assumptions when the observed results do not correspond to the expected consequences. Health conditions in low-income countries are often so extreme that it may be easier to see that our assumptions are wrong. Hence, studies in the poor countries may sometimes lead to knowledge which is also useful in rich countries. The studies of kuru in New Guinea, which secured Gajdusek the Nobel price, is probably the best example of studies in low-income countries which have led to a better understanding of health problems in our part of the world, in this case the neurodegenerative diseases caused by prions. Own interest may be a better basis than charity for prioritising research. International health research is in our own interest to create a more just world order, but may occasionally also provide a better understanding of our own conditions. From Guinea-Bissau we have several times tried to take the experiences back home.

IT IS "WEAK" CHILDREN WHO DIE ...

In 1978, when we started working in Guinea-Bissau, mortality was 50% before five years of age. Everybody knew that malnutrition was the cause of high mortality in low-income countries. It was the "weak" children who died. To quote a leading epidemiologist: "The children whose death might be prevented by measles vaccine are at risk of dying not because of the severity of measles per se, but because they are on the 'road to death' and their nutritional status is so poor that they are likely to die of any infectious disease. Thus, preventing a death (with measles vaccine may) only change the cause of death". The Swedish research organisation SAREC was therefore funding a project to find out what could be done to change the nutritional situation – and to reduce mortality. However, much

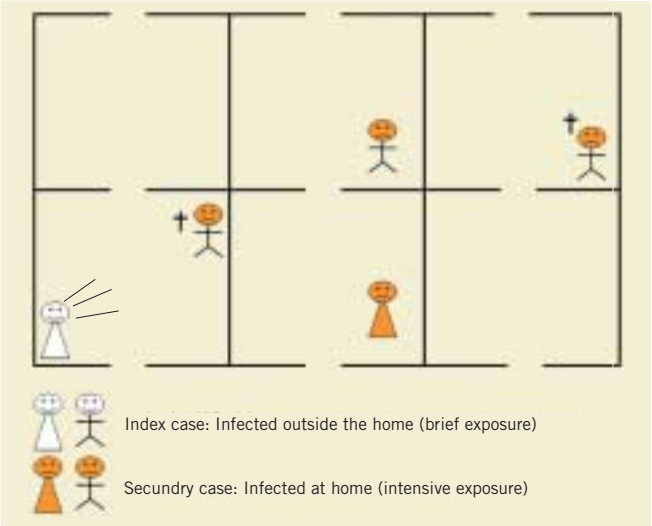


Figure 1. Transmission model for severe measles infection.

to our surprise, the children in Bissau were not malnourished. Nonetheless we observed a case fatality of 21% among children who contracted measles infection. It was not the malnourished children who died of measles. The fundamental mechanism was crowding [1]. Index cases who contracted measles outside the home did not die (Figure 1). However, mortality was high among secondary cases infected at home. All subsequent studies have confirmed this tendency. Intensive exposure is also important for the severity of other childhood infections, including whooping cough, chickenpox and polio. It was not malnutrition but family size and house construction traditions which were the major determinants of mortality. In Bissau, there were 13 persons per house on average. This provided unusual conditions for infecting other children when someone brought an infection home – like living in a kindergarten. More than 60% of the children who contracted measles had been infected at home.

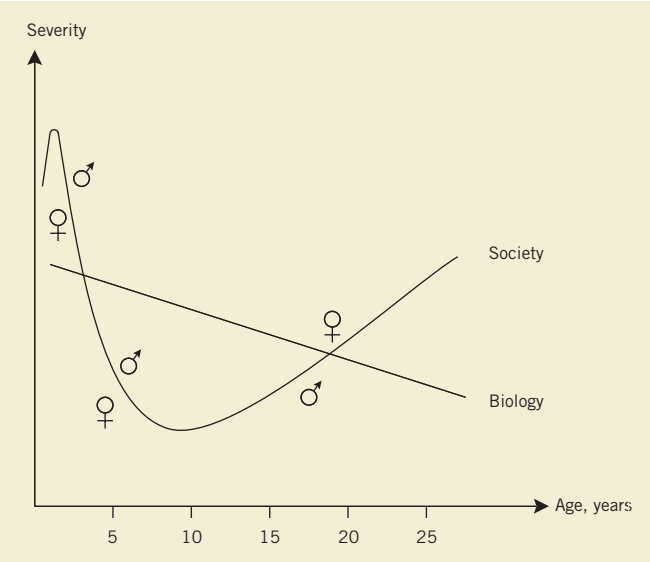
THE DECLINE IN CHILD MORTALITY IN THE INDUSTRIALISED COUNTRIES

The decline in measles mortality in Europe in the period between 1890 and 1940, before antibiotics became available, has been ascribed to better nutrition or a change in the age of infection because families became smaller [2, 3]. The experience from Bissau provided a different perspective on this decline. With the clinical records from Blegdamshospitalet (1915-1925), the infectious disease hospital in Copenhagen, we could show that intensive exposure had also been important in Europe [3]. Mortality at the hospital was 27% (49/183) among 0-2 year old children infected at home but only 7% (10/135) when the record indicated that there were measles cases in the crèche or kindergarten. The children who died of measles were not malnourished. The case fatality was generally lower in years in which many children had been infected in child institutions rather than at home [3]. In contrast to Reves' theory about an increase in the age of infection [2], the age of infection declined in this period even though family size declined. With increasing urbanisation and more child institutions, the number of contacts outside the home would increase and the age of infection should decline. This did happen in England which has the best historical data [3]. Normally the individual risk of dying of an infection is highest for the youngest children and one might therefore have expected mortality to increase in this period with lower age at infection. However, the association does not apply at the population level. The emphasis on intensity of exposure as the main determinant of severity of infection (Figure 1) may provide a different explanation. In England, between 1875 and 1925, family size declined from 6.7 to 2.6 children per women. This reduced tremendously the risk of contracting infection at home. Urbanisation and child institutions increased the risk of

getting infected outside the home with mild infection. Children infected in a kindergarten did not later become a secondary case or infected younger siblings at home. Therefore measles mortality declined even though there was no increase in the age of infection and no antibiotics to treat complications of measles.

POLIO: ELITE OR CROWDING DISEASE

After the polio epidemics in the 1940s and 1950s, it became common knowledge that polio had become more severe because it infected older children. Polio was apparently associated with small families and better social and hygienic conditions. Polio was common among single and firstborn children because they became infected later in life. Hence, the disease was worse in the higher social classes. It was also the common understanding that there was no polio in low-income countries because infection occurred very early in life. The better hygienic conditions at the beginning of the 20th century and the smaller families implied a later age of infection at which it became dangerous. This disease perspective has been called the "polio model" [4] and has often been used to explain "new" chronic diseases as for example multiple sclerosis. These diseases could be new manifestations of common infections which have changed the age of infection. It is doubtful whether the "polio model" applies to polio. Before we introduced polio vaccination in the area in Bissau in 1981, 2% of each birth cohort got permanent paralyses and nearly all had contracted their infection in the first year of life. The records from Blegdamshospitalet showed that there was no special social gradient in polio infection [4]. The disease was not more common in single or firstborn children. It was a crowding disease. Polio was more common in families with several children and among the last born children [4]. The severity curve for polio infection showed a U-formed curve with the most severe cases among the youngest and the oldest children [4, 5] (Figure 2). This U-shape corresponds to the relative frequency of intensively infected children in different age groups. An infection is spread between different families in the age group in which there is frequent contact between susceptible children, i.e. *the age of spread*. Children infected before or after this age will tend to be secondary cases infected at home by siblings belonging to the age of spread. A 100 years ago, the age of spread was the first year in school and the smallest children died of measles when a sibling brought the infection back from school [3]. The age of spread has subsequently moved to kindergartens and crèches. In the Copenhagen polio epidemics the age of spread was 4-5 years of age. In two-child families, the youngest child would tend to be infected if less than four years of age, whereas the older sibling was more likely to be infected after five years of age [4]. The improved hygienic conditions at the beginning of the 20th century created the new polio epidemic not because a new age group was hit but rather because the improved conditions implied that there were many simultaneously susceptible children. When the epidemic occurred polio behaved like a crowding disease with intensive exposure as the most important determinant for severe disease rather than the elite disease of the "polio model".



Figur 2. Severity of childhood infections in relation to age. "Biology" is the expected curve based on vaccinations as an experimental model, severity decreasing with age. "Society" is the observed distribution of severity of infections like measles, whooping cough, chickenpox, and polio. The precise bottom point may vary for different infections. It should be noted that the relative severity for boys and girls varies with age (6).

SHOULD VACCINES BE STOPPED WHEN THE DISEASE HAS BEEN ERADICATED?

If it was not the "weak" children who died of measles there is no reason that children saved from dying of measles by vaccination should die from other causes. We conducted the first measles vaccination campaign in Bissau in 1979 [6]. The result was surprising. Mortality in the age group six months to three years of age dropped to one-third from one year to the next. All later studies including some minor randomised studies have confirmed that measles vaccination is associated with major reductions in mortality. The reduction in mortality cannot be explained by protection against measles infection. This led to the hypothesis that measles vaccine has beneficial immune stimulatory effects [7]. There are many indications that such non-specific effects may be very important. The beneficial effects are particularly important for girls [7]. When WHO introduced a new high-titre measles vaccine in 1989 it was associated with two-fold higher mortality for girls even though the vaccine was fully protective against measles infection [8]. The vaccine made no difference to boys. If the common measles vaccine can have beneficial non-specific effects it raises important questions about our understanding of diseases. The ultimate success in disease control is global eradication and removal of the vaccine. Cost-benefit analyses for smallpox, measles and polio have shown major benefits associated with eradication. However, if the vaccine has beneficial immune stimulatory effects, it is not evident that it will be of benefit to stop vaccination. Mortality may increase when measles is eradicated and measles vaccine removed. What happened when smallpox vaccination was removed? Studies were not conducted when the vaccine was withdrawn in the 1970s. We have subsequently in Guinea-Bissau registered smallpox vaccination scars in several population studies. Even 25 years after the last vaccinations, we found that a smallpox scar was associated with significantly lower mortality particularly for women; the more scars the better [9]. In Denmark we linked the national birth cohort (Better-Health-for-Mother-and-Child) with the school health cards which hold information on vaccination status of the mothers born in the 1960s and 1970s. Smallpox vaccinations were phased out between 1970 and 1976. Women who were smallpox vaccinated had 45% less self-reported asthma than women who were not smallpox vaccinated [10]. Other European studies have shown that smallpox vaccinations are associated with a reduction in the risk of malignant melanoma.

We may understand our childhood infections and vaccinations better by studying them under the extreme conditions in the poorest countries. Maybe we can also understand our chronic diseases better by studying obesity, diabetes and cancer in Asia and Africa. It is in our own interest that there is much more research in international health.

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