

*Contemporary Themes***Benefits and risks of childhood immunisations in developing countries**

JOHN D HOLDEN

Abstract

The ratio of benefit to harm from an imaginary, modest immunisation programme in a developing country and the numbers of lives likely to be saved and severe handicaps prevented have been estimated. Immunisation is much more likely to benefit children than to harm them, and health workers can be confidently encouraged not to withhold the benefits of immunisation from most children.

Introduction

The Expanded Programme on Immunisation is now 13 years old, and the United Nations' target date for immunisation to be available to all the world's children is 1990. UNICEF reports great progress in many countries towards this target¹ and estimates that over 800 000 deaths in children are prevented each year by immunisation. A further estimated 3 450 000 children die each year from diseases that can be prevented by vaccination.

To reduce this number further the emphasis is shifting away from "can this child be vaccinated?" to "the decision to withhold the benefits of immunisation from a child should never be taken lightly."² Many health workers, however, may still be concerned about the dangers of immunisation and do not appreciate that the potential benefits usually far outweigh any risks to the child. Because of their hesitation many children are probably still being deprived of the benefits of immunisation.

A great deal of the information on benefits and risks is difficult to

apply to real life and so uncertainty may remain. To overcome this I have attempted to calculate the benefits and risks of a "typical" immunisation programme in a developing country for each of the six vaccine preventable diseases in the Expanded Programme on Immunisation.

Method

I have imagined a relatively modest immunisation programme, working five days a week for 50 weeks of each year, with the dropout rates that are typical throughout the world—that is, a 40% dropout rate between the first and third doses of diphtheria-tetanus-pertussis and polio.³ I have based my model on a programme giving the doses shown in table I daily and yearly, and the effectiveness is also shown there. For example, I have assumed that the first diphtheria-tetanus-pertussis doses will provide 50% protection and two doses 70% protection, etc. The model programme would vaccinate 120 children daily: 50 on their first visit with bacillus Calmette-Guérin (BCG), diphtheria-tetanus-pertussis, and polio; 40 on their second visit with diphtheria-tetanus-pertussis and polio; 30 on their third visit with diphtheria-tetanus-pertussis, polio, and measles.

TABLE I—The model immunisation programme: typical workload in doses of vaccine administered and assumed effectiveness of vaccine

Vaccine	Doses of vaccine administered		Effectiveness of vaccine ⁴⁻⁸ (%)
	Daily	Yearly	
BCG	50	12 500	Assumed to prevent only tuberculous meningitis and miliary tuberculosis
DTP 1	50	12 500	50
DTP 2	40	10 000	Over 20
DTP 3	30	7 500	Over 20
Polio 1	50	12 500	40
Polio 2	40	10 000	Over 20
Polio 3	30	7 500	Over 20
Measles	30	7 500	90

BCG=Bacillus Calmette-Guérin. DTP=Diphtheria-tetanus-pertussis.

Haydock, Lancashire

JOHN D HOLDEN, MB, MRCP, general practitioner

Correspondence to: Health Centre, Station Road, Haydock, St Helens WA11 0JN.

Results

BCG

Although there is evidence that BCG is highly effective in preventing tuberculosis,⁹ this is still controversial, and I have assumed it is effective only in preventing tuberculous meningitis and miliary tuberculosis. The number of childhood deaths from tuberculous meningitis each year is estimated at 20 000, and approximately 100 million children are born in the developing world each year.¹⁰ This is the basis of my calculation. I have assumed that a further 3000 children die from miliary tuberculosis each year on the basis of figures from Bombay.¹¹ I have assumed that one child is left seriously handicapped for every two that die from the disease.¹²

children aged 1 to 15 years are at particular risk of contracting tetanus.²⁴ I have assumed an incidence of 40 cases per 100 000 children under age 15 a year with a 50% mortality,^{23,24} that the average duration of protection from primary vaccination is 15 years,²⁵ and that there is no residual handicap in survivors of clinical tetanus.²³ I have not included an assessment of additional benefit from prevention of neonatal tetanus. Although the persisting antibodies in many women from vaccination in childhood will be transmitted transplacentally, and thus give their children some protection against neonatal tetanus, this will not directly benefit the recipient of the vaccine herself. I am not aware of any work that would help to qualify the benefit to neonates from their mother's vaccination in childhood.

The results of a study of US Air Force recruits with a history of adverse reaction to tetanus toxoid immunisation showed that all 95 patients with a

TABLE II—*The model immunisation programme: frequency of benefit and frequency of harm (death and serious handicap) and their ratio*

	Benefit from the immunisation programme each year		Frequency of harm from the immunisation programme (by years)		Ratio of benefit:harm	
	No of deaths prevented*	No of serious prevented handicaps*	One death in:	One serious handicap in:	Death	Serious handicap
BCG	3	1	160	80	480:1	80:1
Diphtheria	—	—	?	?	—	—
Pertussis	195	98	41	14	7995:1	1372:1
Tetanus	29	—	>160	>160	>4640:1	?
Polio	3	34	330	33	990:1	1122:1
Measles	338	17	180	260	60 840:1	4420:1
Total No	568	150				

*Numbers are rounded off to nearest whole number.

"The incidence of fatal disseminated BCG infections after routine vaccination has been estimated at one in one million in Scandinavia and one in five million in both Czechoslovakia and the United Kingdom."¹³ I have assumed an incidence of fatal disseminated BCG of one in two million. This takes no account of the fact that many of these children had severe immunological deficiencies and would be in grave danger of overwhelming, fatal infection from many pathogens in most countries. I assume the incidence of BCG osteitis to be one in one million.²

DIPHTHERIA

"For diphtheria, which often occurs as a mild skin infection in developing countries, there is inadequate information on the magnitude of the problem of the life threatening pharyngeal disease."¹⁴ In a rural area of West Bengal, however, diphtheria was the most frequent cause of admission to hospital of children below age 10.¹⁵ In Zambia one hospital reported 22 cases in eight months and three deaths.¹⁶ In Canada from 1924 to 1950 the case fatality rate from diphtheria was approximately 10%.¹⁷

It has been considered probable that "improved nutrition and the general management of cutaneous infections may reduce the incidence of secondary diphtheritic invasion, and the spontaneous active immunisation which accompanies it,"¹⁸ and there is a considerable threat of diphtheria becoming a real problem in unvaccinated individuals in developing countries.

The safety of the vaccine is strongly suggested by the absence of reported deaths from diphtheria/tetanus immunisation throughout the United States in 1979-82.¹⁹

PERTUSSIS

I have assumed that 80% of unvaccinated children contract pertussis,²⁰ that the case fatality rate is 2%,²¹ and that a further 1% of children are left with permanent brain damage.² The most commonly quoted figure for the incidence of persistent serious brain damage after pertussis immunisation is one in 310 000 doses.²² I have assumed that a quarter of these children will die from this complication.

TETANUS

The incidence of tetanus has been estimated to be 10 to 50 cases per 100 000 population a year in many developing countries.²³ In these countries

history suggestive of a prior anaphylactic reaction to tetanus toxoid tolerated full immunising doses of diphtheria and tetanus toxoid.²⁶ Up to 1982, 14 cases of peripheral neuropathy after tetanus toxoid injection were reported in publications world wide.²⁷ I have assumed from these accounts, and from the few reports of death or serious handicap after tetanus toxoid vaccination, that the incidence of both death and serious handicap is not more than one in five million doses. The four year study of adverse events occurring after immunisation in the USA has added support to the conclusion by failing to record any deaths due to tetanus immunisation throughout the country.¹⁹

POLIO

In studies in India,²⁸ the Yemen Arab Republic,²⁹ and Ghana³⁰ prevalence rates of lameness attributable to polio in school age children of 0.32%, 0.40%, and 0.70% have been reported. I have assumed a rate of 0.40% or one lame child out of every 250 susceptible children. In 1954 in the last major poliomyelitis epidemic in England and Wales there were 7776 cases of polio and 700 deaths.³¹ I have assumed that one death will have occurred for every 10 children left lame by polio—that is, one in 2500 susceptible children will die from polio.

A survey in six countries showed 35 cases of poliomyelitis after vaccination of 23 million children.³² In the USA the reported risk of paralysis in those vaccinated or their close contacts was one case per 3.2 million doses distributed.² I have assumed the risk to be one case of paralysis per million doses and the paralysis:death ratio to be again 10:1.

MEASLES

The reported case fatality rates from measles in the developing world vary widely, with rates of 3.7% in one study from Bangladesh³³ and 13.2% after nine months' follow up after measles in the Gambia.⁷ I have assumed a mortality of 5% and that all unvaccinated children will contract the disease sometime in childhood. Measles encephalitis and the precipitation of vitamin A deficiency by measles can lead to serious handicap. I have assumed that one in 400 children will be left with a major handicap such as blindness after measles.^{34,35}

In the USA neurological disorders have been reported once for roughly every million doses of measles vaccine administered² and encephalitis or encephalopathy, or both, 0.3 times per million doses of measles vaccine administered.¹⁹ Deaths were reported 0.7 times per million doses of measles vaccine administered.¹⁹ I have assumed a rate of permanent serious handicap of one in two million doses and death of one in 1 400 000 doses.

The figures and calculations in this study are based on rates of death and serious handicap that apply to economically developing countries. The studies quoted were carried out in countries with an infant mortality of 80 per 1000 or more in 1983¹—that is, 57 countries with a total population of 1764 million—and the ratios of benefit and harm may be assumed to apply to those countries only. In countries with greater prosperity and lower infant mortality the benefits would probably be proportionately fewer, although still substantial in most cases.

Discussion

Table II shows the enormous benefits from five of the six vaccines used in the Expanded Programme on Immunisation, with the sixth, diphtheria, of known value but the size of the problem of classical diphtheria in developing countries being uncertain.

The figures that I have calculated have been slightly rounded off to avoid an impression of a degree of accuracy that is impossible to achieve in such an analysis. For all my assumptions I have tried to err on the side of underestimating the likely benefit of immunisation and overestimating the potential risks of vaccination. Expressed in a different way, this "typical programme" could be expected to save about 45 lives a month and prevent about 12 children being left with a serious handicap each month. In contrast it may cause one death every 22 years and one serious handicap every seven and a half years. The potential benefits to individual children of a much more modest programme would still be considerable, and, of course, regional or national programmes may be expected to have a great impact on deaths and handicap in childhood.

The column in table II of the ratio benefit:harm from immunisation gives figures up to a staggering 60 840:1 for the prevention of deaths from measles. I hope that these figures will convince even the most hesitant healthworkers of the overwhelming probability that each child whom they vaccinate will derive benefit and not harm from the vaccines (provided that the child does not have one of the very few absolute contraindications to the immunisation).

In conclusion I can only re-emphasise this: "The decision to withhold the benefits of immunisation from a child should never be taken lightly."

References

- 1 *The state of the world's children 1986*, UNICEF. Oxford: Oxford University Press, 1986.
- 2 Galazka AM, Lauer BA, Henderson RH, Keja J. Should sick infants be vaccinated? *World Health Forum* 1984;5:269-72.
- 3 Henderson RH. Results of EPI sample surveys of immunisation. Coverage performed during

review of national programmes by year 1975-1983. Geneva: World Health Organisation. Quoted in *The State of the World's Children 1985*, UNICEF. Oxford: Oxford University Press, 1985.

- 4 Greenwood BM, Whittle HC. Immunization. In: Greenwood BM, Whittle HC, eds. *Immunology of medicine in tropics*. London: Arnold, 1981:246-83.
- 5 Nategh R, Naficy K, Shahriary M. Mass trivalent oral polio vaccination in primary school age children in Tehran. *Trop Geogr Med* 1970;22:303-6.
- 6 Poliomyelitis Commission. Poliomyelitis vaccination in Ibadan, Nigeria, during 1964 with oral vaccine (Sabin strains). *Bull WHO* 1966;34:865-76.
- 7 Hull HF, William PJ, Oldfield F. Measles mortality and vaccine efficacy in rural West Africa. *Lancet* 1983;ii:972-5.
- 8 Church MA. Evidence of whooping-cough vaccine efficacy from the 1978 whooping-cough epidemic in Hertfordshire. *Lancet* 1979;ii:188-90.
- 9 Clemens JD, Chuong JJ, Feinstein AR. The BCG controversy: a methodological and statistical reappraisal. *JAMA* 1983;249:2362-9.
- 10 Henderson RH. Vaccine preventable diseases of children: the problem. *Protecting the world's children: vaccines and immunization*. New York: Rockefeller Foundation, 1984.
- 11 Udani PM, Maddocks I. Tuberculosis. In: Jelliffe DB, Stanfield JP, eds. *Diseases of children in the subtropics and tropics*. London: Arnold, 1978:304.
- 12 Viswanathan J. Meningitis. In: Jelliffe DB, Stanfield JP, eds. *Diseases of children in the subtropics and tropics*. London: Arnold, 1978:360-80.
- 13 Mackay A, Alcorn MJ, Macleod IM, et al. Fatal disseminated BCG infections in an 18 year old boy. *Lancet* 1980;iii:1332-4.
- 14 Sabin AB. Strategy for rapid elimination and continuing control of poliomyelitis and other vaccine preventable diseases of children in developing countries. *Br Med J* 1986;292:531-3.
- 15 Chakraborty SM. The incidence and treatment of faucial diphtheria in a rural West Bengali population. *Journal of the Indian Medical Association* 1970;55:371-5.
- 16 Chintu C, Bathirunathan N, Patel JM. Diphtheria at the University Teaching Hospital, Lusaka. *East African Med J* 1978;55:36-8.
- 17 Greenberg L. The use and results of diphtheria immunization. *Bull WHO* 1955;13:367-80.
- 18 Bwibo N. Diphtheria. In: Jelliffe DB, Stanfield JP, eds. *Diseases of children in the subtropics and tropics*. London: Arnold, 1978:257-62.
- 19 Anonymous. Adverse events following immunization. *MMWR* 1985;34:43-7.
- 20 Guérin N. Recent progress in immunization. *Assignment Children* 1983;61/62:123-42.
- 21 Mahieu JM, Muller AS, Voorhoeve AM, Dikken H. Pertussis in a rural area of Kenya: epidemiology and a preliminary report on a vaccine trial. *Bull WHO* 1978;56:773-80.
- 22 Miller DL, Ross EM, Alderslade R, Bellman MH, Rawson NSB. Pertussis immunization and serious acute neurological illness in children. *Br Med J* 1981;282:1595-9.
- 23 Senecal J. Tetanus. In: Jelliffe DB, Stanfield JP, eds. *Diseases of children in the subtropics and tropics*. London: Arnold, 1978:696-704.
- 24 Bytchenko B. Geographical distribution of tetanus in the world, 1951-1960. *Bull WHO* 1966;34:71-104.
- 25 Simonsen O, Kjeldsen K, Heron I. Immunity against tetanus and effect of revaccination, 25-30 years after primary vaccination. *Lancet* 1984;ii:1240-2.
- 26 Jacobs RL, Lowe RS, Lanier BQ. Adverse reactions to tetanus toxoid. *JAMA* 1982;247:40-2.
- 27 Reinstein L, Pargament JM, Goodman JS. Peripheral neuropathy after multiple tetanus toxoid injections. *Arch Phys Med Rehab* 1982;63:332-4.
- 28 John TK, John TJ. Is poliomyelitis a serious problem in developing countries? The Vellors experience. *J Trop Paediatr* 1982;28:11-3.
- 29 Hajar MM, Zeid AS, Saif MA, Parvez MA, Steinglass RC, Crain S. Prevalence, incidence and epidemiological features of poliomyelitis in the Yemen Arab Republic. *Bull WHO* 1981;61:353-9.
- 30 Nicholas DD, Kratzer JH, Ofosu-Amaah S, Belcher DW. Is poliomyelitis a serious problem in developing countries? The Danfu experience. *Br Med J* 1977;274:1009-12.
- 31 Aronson JD, Aronson CF, Taylor HC. A twenty-year appraisal of BCG vaccination in the control of tuberculosis. *Arch Intern Med* 1958;101:881-93.
- 32 Anonymous. The relation between acute persisting spinal paralysis and poliomyelitis vaccine (oral): results of a WHO enquiry. *Bull WHO* 1976;53:319-31.
- 33 Koster FT, Curlin GC, Aziz KMA, Haque A. Synergistic impact of measles and diarrhoea on nutrition and mortality in Bangladesh. *Bull WHO* 1981;59:901-8.
- 34 Reddy V. Vitamin A deficiency and blindness in Indian children. *Indian J Med Res* 1978;68(suppl, October):26-37.
- 35 Franken S. Measles and xerophthalmia in east Africa. *Trop Geogr Med* 1974;26:39-44.

(Accepted 23 February 1987)

A normotensive non-smoking man in his early 20s has a family history of early coronary disease. What can be done to prevent and detect ischaemic heart disease in this man?

The generally accepted coronary artery disease risk factors may be divided into those that are potentially modifiable, such as smoking, hypertension, and hyperlipidaemia and those that are not, such as age, sex, and family history. For a family history to be important there must be evidence of premature death or myocardial infarction in a young first degree relative, but it is important to ascertain the smoking habits of such relatives. Hyperlipidaemia should be sought by examining a serum sample taken from a fasting patient and if the lipid concentration is sufficiently raised (>6.5 mmol/l) you should institute dietary modification and possibly drug treatment (if >7.8 mmol/l).¹ Other preventive measures that anecdotally prevent atherosclerosis include: strenuous exercise, prudent low fat—(possibly vegetarian)—diet, low coffee intake, and reduction in stress. There is no satisfactory method for detecting early and asymptomatic coronary artery disease. Stress or exercise electrocardiography is often advocated but, although it is invaluable for the diagnosis of myocardial ischaemia in patients with chest pain, the high rate of false positive tests (ST depression without underlying coronary artery disease) largely negates its diagnostic value in patients without chest pain.—L M SHAPIRO, senior registrar in cardiology, London.

1 British Cardiac Society working group on coronary prevention: conclusions and recommendations. *Br Heart J* 1987;57:188-9.

Does minoxidil promote the growth of scalp hair in bald men? If so is it an advisable treatment?

More than 10 years of research has gone into assessing the effects of topical minoxidil as a promoter of hair growth; this succeeded the knowledge that 80% of subjects taking oral minoxidil (Loniten) for severe hypertension develop disfiguring hypertrichosis all over the body, including the bald head in some cases. Experience so far shows that a third to a half of men with baldness of an early type (male pattern)—that is, not severely bald and no older than early 30s—grow considerable amounts of hair in the affected area. The Committee on Safety of Medicines has not yet granted a licence for the product, 2% minoxidil solution (Regaine, Upjohn). Those who develop good regrowth notice relapse when the drug is stopped. Whether applying the product continuously for many decades is a good idea remains to be seen, though the topical preparation appears to have no important systemic side effects.—R P R DAWBER, consultant dermatologist, Oxford.

Hern RS. Topical minoxidil: a survey of use and complications. *Arch Dermatol* 1987;123:62-5. *J Am Acad Dermatol* 1987;16, part 2:648-750. (A complete supplement devoted to topical minoxidil.)