

EDITORIAL

***Haemophilus influenzae* type b vaccine in Papua New Guinea: what can we expect, and how should we determine priority for child health interventions?**

The *Haemophilus influenzae* protein conjugate vaccines are effective at preventing disease and death from *Haemophilus influenzae* type b (Hib) pneumonia and meningitis in children in developing countries (1). Much of the early research that determined the aetiology of pneumonia and meningitis, and the central role of *Haemophilus influenzae*, was done in Papua New Guinea (PNG) (2). Until the 1990s the only defence against Hib disease was standard antibiotic treatment, particularly chloramphenicol for severe infections. Now the incidence of chloramphenicol-resistant Hib in isolates from cerebrospinal fluid is as high as 30%. What impact can we expect from Hib vaccine, at what cost, and what other vaccines do we need to reduce the unacceptably high child mortality rate in PNG?

I propose that we should determine the relative priority of any new health intervention by 1) the proportional reduction in mortality and 2) the cost per life saved. In PNG, because mortality is the paramount child health problem, any new strategy must be judged on the reduction in mortality that will result from it, and from the cost relative to other interventions that would produce similar mortality reductions. We must apply the best available evidence and a cost-benefit argument when estimating the magnitude of benefit of any health intervention, including Hib vaccine.

What reduction in child mortality rate in PNG can we expect from Hib vaccine? In the trial in The Gambia mortality was 6.1% lower in vaccine recipients than in control children (1). This occurred, however, in relatively ideal trial circumstances with very good curative health services, and consequently there was a low mortality rate in the control group (6.1 per 1000 children). The effect of Hib vaccine on child mortality in any region will depend upon 1) the frequency of Hib disease, 2) the vaccine coverage achieved and 3) the quality of curative health services. Although it is often

said that about 40% of all cases of pneumonia are due to *Haemophilus influenzae*, only 7% of severe pneumonia in PNG is due to serotype b (2). The other 33% are due to other serotypes and nontypable *Haemophilus*. Unlike most vaccine-preventable diseases, where antibiotics do not make a substantial impact on the outcome of the disease being prevented, the more widespread the application and accessibility of standard treatment for childhood pneumonia, the lower will be the net effect of Hib vaccine on mortality. This is because children with Hib pneumonia treated with appropriate antibiotics and oxygen have a very low mortality. At Goroka Hospital only one death (out of 46) in a series of 750 children with severe pneumonia has been linked to Hib (unpublished data).

In PNG curative health services in rural areas have deteriorated (3): the aid post system has collapsed, many health centres open sporadically, procaine penicillin has been withdrawn, benzylpenicillin is in short supply and supplemental oxygen is poorly administered in most rural health facilities. Most child deaths occur at home without the child receiving good medical care. As we are currently failing to deliver health services to children when they become ill, the potential reduction in pneumonia mortality from Hib vaccination is very high.

What about meningitis? Even when children with Hib meningitis receive appropriate antibiotics and reasonable supportive care, 10-20% still die, and one-third of survivors are left with severe neurological sequelae. No matter how good the peripheral curative health services could become, deaths and permanent disability from Hib meningitis will only be prevented by a primary prevention strategy.

So how many deaths might be prevented by Hib vaccine? Extrapolating from disease aetiology studies we can estimate that there are 11 deaths from Hib disease for every 1000 live

births throughout PNG (5 due to pneumonia and 6 due to meningitis). This is out of an under-5 mortality of 120/1000. There are 150,000 births in PNG annually, therefore about 1650 deaths (150 x11) from Hib disease. If one assumes 80% effective coverage, with a vaccine efficacy of 98% (1) (1650 x 0.8 x 0.98=1294), and allowing for the one-third of all child deaths that occur in the neonatal period and early infancy, a reduction of 860 deaths in children under 5 years of age could be achieved (1294-[1294/3]=863). This is similar to the projected mortality reduction using data from The Gambia (1), where a 6% mortality reduction (in vaccine recipients, who by definition had survived the neonatal period) would mean 720 deaths prevented in PNG (150 x 80 x 0.06=720).

What of the cost? PNG may be able to buy Hib vaccine for about US\$2.50 per dose. With a 2-dose regimen (assuming 20% vaccine wastage and 80% effective coverage) the approximate cost per life saved would be US\$870 (K2600)([2.5 x 2 x 1.25 x 150,000 x 0.8]/860=872) (Table 1). This compares

favourably with the situation in The Gambia, where 2686 children needed to be vaccinated to save one life, and the cost per life saved (given the same unit cost of US\$2.50) was US\$13,430 (1).

A major problem is that the quality of vaccine delivery services, which are essential for effective distribution of Hib vaccine, are not independent of the quality and coverage of curative health services. In rural PNG both curative health services and vaccine delivery are poor. In addition to the above health infrastructure problems, the vaccine cold-chain has broken down. Therefore, optimal reduction in child mortality from standard treatment of pneumonia and from Hib vaccination will depend heavily on improvements in basic health services.

It is undoubtedly a worthy endeavour to save 860 young lives each year in PNG, but how does the cost-effectiveness of Hib vaccine compare with other interventions that could and should be done? I suggest some comparative examples. Since August 1998

TABLE 1

THE MOST CONSERVATIVE ESTIMATES OF THE MORTALITY REDUCTIONS THAT WOULD BE ACHIEVED BY VACCINATION AGAINST THE THREE MOST IMPORTANT CAUSES OF CHILD MORTALITY IN PNG

Pathogen and vaccine	Reduction in total mortality	Children vaccinated	Lives saved per year	Doses x cost (US\$)	Cost per life saved
<i>H. influenzae</i>	5%	80%	860	2x\$2.50	US\$870 (K2600)
Measles	30%*	80%	1000*	2x\$0.30	US\$30 (K90)
<i>S. pneumoniae</i>	13%	80%	1820	#	
Total	48%	80%	3680		
	(Under-5 mortality down from 120 to 62 per 1000 live births)	(for 2 doses of three vaccines)			

* The minimum reduction that would be achieved, with a range up to 86% mortality reduction, and 2800 lives saved per year
 # Cost of pneumococcal vaccines will depend on the strategy adopted: options include 1) maternal vaccination followed by infant vaccination (at 9 months of age) both with 23-valent polysaccharide vaccine (estimated cost per life saved US\$180); 2) young infant vaccination with conjugate pneumococcal vaccine (when available), then followed by polysaccharide vaccine at 9-12 months

there has been a measles epidemic in highlands PNG and measles is now one of the most frequent causes of child death. The epidemic has occurred because of inadequate vaccine coverage. Recently it has been shown that measles vaccine has an important nonspecific effect of mortality reduction, apart from protection against death from measles. In a meta-analysis of studies of standard-dose measles vaccine that reported mortality, the protective efficacy against death after measles immunization ranged from 30% to 86% (4) (while the overall mortality burden from measles may only be 10%). Current measles vaccine coverage throughout PNG is about 40-50%. Therefore 50-60%, or about 75,000 (0.5 x 150,000), of the babies born each year are not accorded this important nonspecific protection. If measles coverage were to increase to 80%, then an extra 30-40%, or more than 40,000 children (excluding those who die in early infancy), would be given this protection (0.3 x [150,000-6000]). Of these 43,000 children 3440 (80 per 1000) will die before the age of 5 years. If measles vaccine coverage could be increased to 80%, this nonspecific protection, which would lead to at least a 30% reduction in mortality, would prevent 1000 deaths each year in PNG. The cost of measles vaccine is US\$0.30 and with 2 doses the theoretical cost per life saved would be US\$30 (K90) (after buying the additional vaccines, allowing for 20% vaccine wastage: $[40,000 \times 2 \times 0.3 \times 1.25]/1000 = \text{US\$}30$) (Table 1). This makes measles immunization 30 times more cost-effective than immunization against Hib (Table 1). So it can be seen that more effective delivery of the services that are supposed to currently exist would have a greater impact on child mortality, at a far lower cost, than Hib vaccine. It would make sense for both interventions (Hib and measles) to be done in parallel, as better coverage of existing vaccines is an essential prerequisite for successful introduction of Hib vaccine.

A cost evaluation that only factors in mortality underestimates the cost-effectiveness of the vaccine. Other benefits from Hib vaccination would be a substantial reduction in hospital admissions from pneumonia (20% in the Gambian trial), reduction in the number of children with severe neurological sequelae following Hib meningitis, and cost-saving on

antibiotics and oxygen (although the latter is currently so poorly provided that there may be no saving in real terms). In addition Hib vaccine may provide an incentive for improving general vaccine coverage. On the other hand, additional costs of infrastructure building, re-establishment of the cold-chain, vaccine patrols and other overheads will be more expensive than the purchase price of the vaccine (5) (but these must be done anyway, regardless of whether Hib is introduced). Currently we have a very expensive, inefficient system where the cost per life saved is far greater than it should be. As the efficiency of a vaccination program increases, the cost per life saved will be substantially reduced (5).

Perhaps the most important benefit of a successful introduction of Hib vaccine is that it would pave the way for introduction of vaccine strategies against *Streptococcus pneumoniae*, the major cause of child mortality in PNG. *S. pneumoniae* causes about 20 deaths per 1000 live births in PNG (14 due to pneumonia and 6 from meningitis). This means that about 3000 children die each year from pneumococcal disease (20 x 150). The 23-valent pneumococcal polysaccharide vaccine has already been shown to reduce total child mortality by 19% in a trial in PNG (6,7) (potentially preventing 1800 deaths annually if 80% coverage could be achieved: $150 \times 80 \times 0.19 \times 0.8 = 1824$). This vaccine, unfortunately, has not been adopted for use (8). Other promising strategies include maternal immunization with polysaccharide vaccine, and new protein-conjugate pneumococcal vaccines in young infants (Table 1). These strategies will be more complex, and the protein-conjugate pneumococcal vaccine will be even more expensive than Hib vaccine, but pneumococcal disease prevention will produce a far greater mortality reduction than prevention of Hib disease. We must explore the wider use of the cheaper polysaccharide vaccine (8). A national Health Department plan for introduction of pneumococcal vaccination is urgently required.

Health administrators and government need to see the paramount importance of pneumonia prevention, and recognize that this entails new and more obvious costs (although there may be a net cost saving in the overall health budget

by disease prevention and a more efficient system). At present the costs of (inadequate) pneumonia control are hidden within the Health Department's budget for drugs, oxygen, staff salaries, health facility maintenance etc. Despite this enormous expenditure on curative health, the battle against pneumonia and meningitis is being lost. For those who would argue that the vaccination strategies proposed here are not affordable, there is now much strong evidence that preventing child mortality is a cost-effective intervention for a developing country (9).

A vision for child health in PNG in the next decade must involve improvement of basic services so that measles, Hib and pneumococcal vaccines can be effectively given to the entire child population. This would result in a decrease in the under-5 mortality rate from 120 per 1000 live births to at least as low as 62 per 1000 live births, and the saving of 4000 young lives each year (Table 1). Only then will we be able to truly say that successful efforts are being made to deal with the major causes of child mortality in PNG.

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