

## Child Health

### THE CASE FOR GLOBAL MEASLES ERADICATION

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**Summary** The global eradication of measles is desirable because the disease occurs almost universally, affects large numbers of children, can cause serious complications, and is responsible for about 900 000 deaths a year in developing countries. The feasibility of a measles eradication programme is suggested by the success of smallpox eradication, the availability of a heat-stable, cheap, and effective vaccine, and the fact that interruption of measles transmission has been achieved in some places. Eradication of measles globally would also result in the saving of the large sums of money being spent on measles treatment, vaccination, and surveillance.

#### INTRODUCTION

THE purpose of this paper is to advocate establishing global measles eradication as a goal, to be achieved by accelerated implementation of the World Health Organisation's (W.H.O.) Expanded Programme on Immunisation (EPI). Eradication of measles is desirable from humanitarian and fiscal grounds, and it is feasible on technical and epidemiological grounds.

#### IMPACT OF MEASLES ON HEALTH

Measles is a major epidemic disease, particularly in children. Except in isolated populations, measles is nearly universal, and most persons are infected before the age of 15. Measles causes serious complications, particularly diarrhoea, encephalitis, otitis media, pneumonia, exacerbation of protein energy malnutrition, and death.<sup>1</sup> Death following measles is especially common in malnourished children in the developing world.<sup>2</sup> Therapy for measles and its complications is a major drain on medical care resources in most parts of Africa, Asia, and Latin America.

Walsh and Warren estimate that approximately 900 000 deaths from measles occur each year in the developing world.<sup>3</sup> Measles is one of the leading causes of death of young children in many countries; it is the leading cause, or the second leading, cause of death in children aged 1-4 in several Latin American cities.<sup>4</sup> Measles outbreaks in Africa and Asia have case-fatality rates of 10-20% in children aged 1-4 years, many of whom are malnourished.<sup>2,5</sup>

Measles complications may also result in developmental retardation, life-long handicaps, and both direct and indirect economic loss. Furthermore, in the developing world, measles interacts with diarrhoeal disease and malnutrition to increase the morbidity and mortality from these conditions. The economic toll taken by measles, and the health effects it causes, should be reduced to the lowest level possible.

#### PROSPECTS FOR MEASLES ERADICATION

The introduction of live measles virus vaccine in 1963 had a profound impact on the occurrence of measles in the

United States<sup>6</sup> and in other countries where it has been applied in an organised and widely supported programme.<sup>7</sup> However, the vaccine has not enjoyed the widest possible use because it used to be expensive and to require a smoothly functioning cold chain to preserve the viability of the vaccine virus, and because measles is not viewed as a serious problem in some countries.

Measles can be controlled, indeed eradicated, by widespread and logical application of vaccine. Three factors support this concept: measures to eradicate smallpox have been successful; measles vaccines that are more heat stable than earlier vaccines are now available; and experience has been gained in efforts to interrupt measles transmission in the United States<sup>8</sup> and Africa.<sup>9</sup>

#### Prospects Based on Success of Smallpox Eradication

The success of the smallpox eradication program<sup>10</sup> suggests that global eradication of measles is also possible, because there are many similarities between measles and smallpox. Both viruses cause infections which are accompanied by typical rashes and which confer life-long immunity; and both viruses have no animal reservoir and do not produce a chronic carrier state in man. However, important differences between them preclude the drawing of exact parallels between smallpox eradication and measles eradication.<sup>11</sup> The first is the highly contagious nature of measles, which is capable of causing explosive outbreaks and spreading rapidly. Typically, three-quarters of susceptible household contacts will be infected on initial exposure.<sup>12</sup> Smallpox generally spreads more slowly and can be contained by aggressive outbreak control measures. Usually, only one-third of susceptible household contacts are infected after initial exposure to smallpox.<sup>13</sup> This difference in contagiousness suggests that an essential ingredient of any measles eradication programme would be the achievement and maintenance of very high immunisation levels, probably in excess of 90%, whereas smallpox was eradicated by outbreak and case containment in many areas, with general immunity rates of less than 50%.<sup>10</sup> Thus a measles eradication programme probably cannot be as focused in its efforts as was the smallpox eradication programme; measles immunisation would have to reach virtually all parts of the country simultaneously and successfully.

A second important difference is that the average age at which infection with smallpox occurs tended to be 4-5 years old or more, whereas measles infection in the developing world generally affects those 12-18 months of age. Also, smallpox vaccine is safe and effective when given to newborn infants, but measles vaccine is not effective if given before the 6th or 9th month of life because of interference by maternal antibody; indeed maximum seroconversion may not occur in some populations until the age of 12-15 months.<sup>14</sup> Thus a permanent primary-care infrastructure capable of routinely delivering vaccines to the majority of the population is necessary to eliminate measles transmission. Smallpox eradication was in many areas accomplished by an intermittent or itinerant immunisation campaign, without a permanent primary-health-care infrastructure.

A third difference is that measles surveillance is more difficult than smallpox surveillance. Measles is more readily confused with other illnesses that produce a rash, and mild cases are more likely to be missed. Surveillance is the primary tool for evaluating the effectiveness of vaccine campaigns, and good surveillance data are necessary to shape adjustments and improvements in the programme. The difficulties of

measles surveillance may impede the effectiveness of special operations when the number of residual cases becomes increasingly small.

The fourth difference is that those who have acquired immunity to smallpox can be easily recognised by the vaccination scar or by pockmarks, but those immune to measles are not so easily identifiable. Determination of the true prevalence of immunity to measles in communities may thus require occasional serological surveys unless very good records are available. Such surveys would add to the logistic and laboratory costs for a measles eradication programme.

#### *Prospects Based on Availability of Heat-stable, Cheap, and Effective Vaccine*

Two constraints to controlling or eradicating measles in developing countries used to be the sensitivity of the vaccine to heat, and its high cost. The constraints have been considerably eased by the development of a vaccine which can remain potent in the freeze-dried state at ambient tropical temperatures for 3 to 4 weeks,<sup>15</sup> by the availability of containers which can maintain vaccines at low temperatures, and by the reduction in the cost of measles vaccine to the current W.H.O. price of U.S.\$2 for a 20-dose vial.

These improvements are helpful, but the administration of measles vaccine, by a sterile needle and syringe or by jet injector gun, is not as convenient and cheap as the administration of smallpox vaccine, which is given by intradermal inoculation with the bifurcated needle. Moreover, in developing countries, it is more difficult to establish high standards of quality control for the production of measles vaccine than it was for smallpox vaccine, which is produced by a simpler process.

Measles vaccine is quite effective; it generally produces complete immunity in more than 90% of the recipients when given at or after 9 months of age. Age at vaccination should vary by country and region, and depends on the persistence of maternal antibodies and the age-specific incidence of measles. In the United States, for reasons which are not totally understood, seroconversion rates in 9-month-olds are lower than when vaccine is administered after the first birthday.<sup>14</sup> The age at which vaccine is given might be addressed by a W.H.O. expert advisory group. Fortunately, there are essentially no contraindications or serious side-effects which hamper the widespread application of measles vaccine.

#### *Prospects Based on Experience with Interruption of Measles Transmission*

Despite the likelihood that worldwide measles eradication would be more difficult than smallpox eradication, recent successes in interrupting measles transmission and both technical and administrative advances make measles eradication practical. Sizeable geographic areas have been maintained measles-free by a programme of routine immunisation, aggressive surveillance, and outbreak control. During the regional Smallpox Eradication/Measles Control Program in West and Central Africa in the late 1960s and early 1970s, The Gambia, with a population of about 350 000 persons, eliminated reported measles, and for over 2 years maintained a measles-free state, other than for occasional, imported cases which were rapidly controlled.<sup>9</sup> Recent experience in the United States indicates that large portions of the country are already free of indigenous measles transmission<sup>8</sup>—during 1980, 77% of the 3144 counties in the United States were free of measles for the entire year; and provisional data for 1981 indicate that 90% of the counties were free of measles for the entire year.<sup>16</sup> The U.S. is making

steady progress towards its goal of eliminating indigenous transmission of measles by October, 1982.

#### IMPLEMENTATION OF A MEASLES ERADICATION PROGRAMME

Given that the mortality and morbidity of measles are considerable, and that the prospects for measles eradication are encouraging, consideration of global eradication of measles is inevitable. In fact, a mechanism for achieving this goal already is being developed: the global Expanded Programme on Immunization (EPI) coordinated by the World Health Organisation. The EPI is successfully working with national governments and international donor agencies towards making childhood immunisations (diphtheria, pertussis, tetanus, polio, BCG, and measles) routinely available to all children by 1990. The goal of the EPI is at present stated in terms of service delivery, but morbidity targets will soon be established.<sup>17</sup> Measles eradication seems to be an appropriate goal for the programme.

We believe it would be easier to eradicate measles by an intensive early effort in a limited period, rather than by a gradual effort over a prolonged period. Partial vaccination of the target population may change the epidemiology of measles such that susceptible persons may become dispersed in the population.<sup>6</sup> In endemic areas, most individuals are infected with measles before their 3rd to 5th birthday, and the target group of susceptible children can easily be defined as those aged between 9 months and 5 years. Vaccination efforts can be directed toward this group. A point to beware of is that imperfect coverage by a vaccination programme may result in the accumulation of susceptible individuals in older age groups because, as some children are immunised, the rate of infection declines, and some individuals may enter late childhood without having been infected or vaccinated. Since persons who are susceptible to measles cannot be as readily identified as those susceptible to smallpox, it will be more difficult to ensure that remaining susceptible individuals are vaccinated than was the case during the Smallpox Eradication Program. Near universal vaccination of those less than 5 years old would prevent this problem.

#### BENEFITS TO DEVELOPED WORLD OF GLOBAL ERADICATION OF MEASLES

It is the interests of not only the developing world but also the developed world that would be served by global eradication of measles. For instance, in many developed countries immunisation levels are high enough to reduce measles incidence to a point where the disease persists but is no longer a constantly visible problem. In England, for example, measles vaccine acceptance in children is approximately 50%, and stable numbers of measles cases and deaths continue to occur each year (average 125 000 cases per year in the period 1971 to 1980, inclusive, and 24 deaths per year in the period 1971 to 1977, inclusive).<sup>18,19</sup> Although this represents a 70% decline in cases and deaths compared with that in the immediate pre-vaccine era, a concerted public health effort could further reduce unnecessary death and disability from measles in England.

Even in places where indigenous measles transmission has been eliminated, such as in the United States, the nation's costs of routine measles vaccination, surveillance, and response to imported cases will be approximately \$10–25 million per year (total of private sector and public sector costs). The earlier the global target is achieved, the earlier the United States can discontinue these costs. It cost the U.S. a considerable sum (\$124 million a year) to keep itself free of

smallpox for more than a quarter of a century before the global Smallpox Eradication Program began. The \$32 million which the U.S. invested in the Smallpox Eradication Program over 10 years was thus recouped every 3 months once global progress against smallpox meant that she could discontinue routine vaccination and other activities related to protection against smallpox.<sup>20</sup> The prevention of measles by vaccination was estimated to yield an annual net saving of \$130 million from 1963 to 1972 in the United States.<sup>21</sup> Current annual savings are estimated to be approximately \$500 million. Measles vaccination in the United States is estimated to have a benefit:cost ratio of 10 to 1. (The return on investment in the developing world, where morbidity and mortality for measles are higher, would be even greater—a preliminary analysis of vaccine programmes in the Ivory Coast suggests the benefit to cost ratio may well exceed 20 to 1 [Shephard DS, personal communication].)

#### EFFECTS OF FAILURE OF A MEASLES ERADICATION PROGRAMME

One must always consider the risk of failure. If global measles eradication is not achieved by the EPI, efforts to protect against measles will have to continue. However, if a measles eradication programme did not reach its target on schedule, the world would nonetheless be a healthier place, with millions of children protected not only from measles, but also from diphtheria, pertussis, polio, and tetanus. The structure to deliver other needed immunisations and indeed other aspects of primary health care will be promoted rather than jeopardised by an early vigorous attempt to eradicate measles.

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#### REFERENCES

- Krugman S, Katz SL. Infectious disease of children. St. Louis: C. V. Mosby, 1981.
- Morley D, Woodland M, Martin WJ. Measles in Nigerian children. *J Hyg Camb* 1963; **61**: 115-34.
- Walsh JA, Warren KS. Selective primary health care: An interim strategy for disease control in developing countries. *N Engl J Med* 1979; **301**: 967-74.
- Puffer RR, Serrano CV. Patterns of mortality in childhood. Report of the Inter-American investigation of mortality in childhood. Pan American Health Organization. Scientific Publication No. 262. Washington, 1973.
- John TJ, Joseph TI, Radhkrishnan J, Singh RPD, George K. Epidemiology and prevention of measles in rural south India. *Ind J Med Res* 1980; **72**: 153-58.
- Hinman AR, Brandling-Bennett AD, Nieberg PI. The opportunity and obligation to eliminate measles from the United States. *JAMA* 1979; **242**: 1157-62.
- Sejda J. Evaluation of the eight-year period of compulsory measles vaccination in the Czech Socialist Republic (CSR). *J Hyg Epidem Microbiol Immunol (Praha)* 1979; **23**: 273-83.
- Hinman AR, Eddins DL, Kirby CD, et al. Progress in measles elimination. *JAMA* 1982; **247**: 1592-95.
- Forge WH. Measles vaccination in Africa. Proceedings of the international conference on application of vaccines against viral rickettsial, and bacterial diseases of man. Pan American Health Organization Scientific Publ. No. 226, 1971.
- World Health Organization. The Global Eradication of Smallpox. Final Report of the Global Commission for the Certification of Smallpox Eradication. Geneva, 1980.
- Hinman AR. World eradication of measles. *Rev Inf Dis* (in press).
- Hope-Simpson RE. Infectiousness of communicable disease in the household (measles, chickenpox, and mumps). *Lancet* 1952; **ii**: 549-52.
- Sommer A, Foster SO. The 1972 Smallpox Outbreak in Khulna Municipality Bangladesh. *Am J Epidemiol* 1974; **99**: 291-301.
- Centers for Disease Control. Measles—Florida. *Morbidity Mortal Wkly Rep* 1981; **29**: 625-28.
- McAleer WJ, Marcus HZ, McLean AA, Buynah EB, Hilleman MR. Stability on storage at various temperatures of live measles, mumps, and rubella virus vaccines in new stabilizer. *J Biol Standard* 1980; **8**: 281-87.
- Centers for Disease Control. Measles—United States, 1981. *Morbidity Mortal Wkly Rep* 1982; **31**: 37-39.
- World Health Organization. Expanded programme on immunization. Global Advisory Group Meeting. *Weekly Epidem Rec* 1981; **56**: 9-15.
- P.H.L.S. Communicable Disease Surveillance Centre. Measles surveillance 1961-80. *CDR* 1981 81/40 3.
- World Health Organization. World Health Statistics Annuals, 1961-1979.
- Axnick NW, Lane JM. Costs associated with the protection of the United States against smallpox. *WHO/SE/72*, 45, 1972.
- Witte JJ, Axnick NW. The benefits from 10 years of measles immunization in the United States. *Publ Hlth Rep* 1975; **90**: 205-07.

## Occasional Survey

### XANTHOGRANULOMATOUS PYELONEPHRITIS: A REAPPRAISAL

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**Summary** A survey was undertaken of the clinical, radiological, ultrasonic, and pathological features of 80 patients with xanthogranulomatous pyelonephritis (XPN). The condition is a progressive granulomatous reaction to chronic renal inflammation which is often suppurative and usually caused by calculous urinary tract obstruction. The characteristic pathological features are large numbers of foam cells containing lipid, and the presence of inflammatory destruction of neighbouring renal tissue. XPN, which is commoner than generally recognised, may often be diagnosed preoperatively—the patient is usually a middle-aged female who presents with severe toxæmia, tender loin mass, and mild lower urinary tract symptoms. The diagnosis is confirmed by radiology and ultrasonography. Nephrectomy is curative.

#### INTRODUCTION

XANTHOGRANULOMATOUS pyelonephritis (XPN) is a morphological variant of pyelonephritis characterised by the accumulation of large numbers of lipid-laden macrophages in inflamed and often suppurating areas of renal tissue. The solid areas of closely packed foamy macrophages seen in some stages of XPN have been mistaken for the clear cells of renal carcinoma. Incorrect diagnoses are now less common as awareness of this similarity has increased. XPN usually affects the renal pelvis and calyces, and the xanthogranulomatous areas are visible macroscopically, although their presence can easily be missed by casual examination.

The term xanthogranulomatous pyelonephritis was first suggested by Østerlind,<sup>1</sup> but the condition had probably been described by Schlagenhauser<sup>2</sup> and Putschar.<sup>3</sup> Although awareness of XPN has increased in recent years, it is still regarded as rare, and in previous reports only occasional cases were diagnosed preoperatively.

In 1973, only about 100 cases of XPN had been described in the world literature, and these were comprehensively reviewed by Gingell et al.<sup>4</sup> Since then there have been reports of isolated cases<sup>5-8</sup> and a few series, some small,<sup>9-13</sup> others more substantial.<sup>14,15</sup>

Our series of 80 patients is the largest yet reported from a single centre, and it indicates that the condition is considerably more prevalent than previously thought. In our experience, it should now be possible to diagnose XPN preoperatively in a considerable proportion of cases from clinical, laboratory, and organ-imaging findings.

#### PATIENTS

80 patients with histologically proven XPN have been reviewed. 77 cases were collected from Sheffield teaching hospitals and the