Research

Evaluating the impact of the HIV pandemic on measles control and elimination

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Objective To estimate the impact of the HIV pandemic on vaccine-acquired population immunity to measles virus because high levels of population immunity are required to eliminate transmission of measles virus in large geographical areas, and HIV infection can reduce the efficacy of measles vaccination.

Methods A literature review was conducted to estimate key parameters relating to the potential impact of HIV infection on the epidemiology of measles in sub-Saharan Africa; parameters included the prevalence of HIV, child mortality, perinatal HIV transmission rates and protective immune responses to measles vaccination. These parameter estimates were incorporated into a simple model, applicable to regions that have a high prevalence of HIV, to estimate the potential impact of HIV infection on population immunity against measles.

Findings The model suggests that the HIV pandemic should not introduce an insurmountable barrier to measles control and elimination, in part because higher rates of primary and secondary vaccine failure among HIV-infected children are counteracted by their high mortality rate. The HIV pandemic could result in a 2–3% increase in the proportion of the birth cohort susceptible to measles, and more frequent supplemental immunization activities (SIAs) may be necessary to control or eliminate measles. In the model the optimal interval between SIAs was most influenced by the coverage rate for routine measles vaccination. The absence of a second opportunity for vaccination resulted in the greatest increase in the number of susceptible children.

Conclusion These results help explain the initial success of measles elimination efforts in southern Africa, where measles control has been achieved in a setting of high HIV prevalence.

Keywords HIV infections/complications; Measles vaccine; Measles/immunology/epidemiology; Antigen-antibody reactions; Child; Models, Statistical; Africa South of the Sahara (*source: MeSH, NLM*).

Mots clés Infection à VIH/complication; Vaccin antimorbilleux; Rougeole/immunologie/épidemiologie; Réaction antigène-anticorps; Enfant; Modèle statistique; Afrique subsaharienne (*source: MeSH, INSERM*).

Palabras clave Infecciones por VIH/complicaciones; Vacuna antisarampión; Sarampión/inmunología/epidemiología; Reacciones antígeno-anticuerpo; Niño; Modelos estadísticos; África del Sur del Sahara (*fuente: DeCS, BIREME*).

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Introduction

Despite the availability of a safe and effective vaccine against measles, 614 000 measles-related deaths were estimated to have occurred in 2002, making measles a leading cause of childhood death (*1*). WHO, UNICEF, and other partners have established goals to reduce by half the number of measles deaths by 2005 and to interrupt indigenous measles-virus transmission in large geographical areas (*2*). To achieve these mortality-reduction goals, a high level of protection, or population immunity, is required. In areas without circulating measles virus, population immunity is determined by multiplying the proportion of the population vaccinated by the vaccine's effectiveness. In order to achieve a high level of population immunity, control programmes should sustain at least 90% coverage with a first dose of measles vaccine. In addition, a second opportunity for measles vaccination must be provided through routine or supplemental

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activities and reach at least 90% of children. To eliminate measles in large geographical areas, even higher population immunity may be needed (93–95%) (*2–5*). Measles control programmes may have little margin for even small increases in the number of susceptible people such as those that may occur in areas of low vaccination coverage or with reduced vaccine effectiveness.

One of the potential obstacles to measles control and elimination is the HIV pandemic (*6*, 7). Almost half of all measles-related deaths occur in sub-Saharan Africa, and 64% of the world's 40 million people infected with HIV live in the same area (*8–10*). Infection with HIV may modify the clinical manifestations of measles, thus disrupting case–finding efforts, and HIV infection may also alter the communicability of measles by prolonging the infectious period. Most importantly, HIV infection may result in high rates of primary and secondary measles vaccine failure after immunization, resulting in lower vaccine effectiveness.

Despite these potential barriers, progress towards measles elimination in seven countries in southern Africa shows that excellent control of measles can be achieved in regions with high prevalence of HIV infection. This was accomplished by maintaining high routine vaccination rates (average rate = 80%; range = 61–90%) coupled with high coverage in periodic supplemental campaigns (average = 91%; range = 60–105%) (*11*). Reported measles-related deaths fell from 166 in 1996 to 0 in 2000 and 2001. Between 2000 and 2002, these countries reported record low levels of measles; between January 2000 and December 2002, less than 10% (492) of 5113 suspected cases of measles for whom blood results were available were serologically confirmed (*12–14*).

To understand better the interaction between HIV and measles, the factors that have contributed to the success in southern Africa, and what potential barriers might lay ahead, we developed a simple model, applicable to regions in sub-Saharan Africa where there is a high prevalence of HIV, to estimate the impact of the HIV pandemic on population immunity to measles.

Methods

The published literature was reviewed (using MEDLINE and searching keywords including measles, measles vaccination, HIV, AIDS, child mortality) to estimate parameters important in assessing the impact of HIV on population immunity to measles. These parameters included the prevalence of HIV infection in children in sub-Saharan Africa and their likelihood of survival to the age of 5 years, the mode and timing of HIV transmission from mother to infant, the loss of protective maternal antibodies in children born to HIV-infected women, the proportion of HIV-infected children and uninfected children who develop protective immunity following measles immunization, and the duration of this protective immunity.

We constructed a simple model of the impact of the HIV pandemic on population immunity to measles in children less than 5 years old (Appendix 1). This model was designed to illustrate the impact of the HIV pandemic on the proportion of the population that acquires immunity via vaccination; it does not assess the dynamic effects on measles-virus transmission, such as prolonged infectivity. To estimate age-specific rates of measles immunity both in children infected with HIV and those who were not infected we made conservative assumptions about the response of HIV-infected individuals to vaccination (Box 1).

Box 1. **Assumptions of the model**

1. Immunity to measles is a result of vaccination and not infection with wild-type measles virus.
2. The proportion of children who develop protective antibody titres after vaccination at the age of 9 months are:
   a) 65% of children infected with HIV
   b) 85% of children not infected with HIV (*15*).
3. The proportions of children who are assumed to remain protected against measles after vaccination are shown below.
   a) Among HIV-infected children: 50% are protected at 24 months old, 30% at 36 months old, 20% at 48 months old, and 20% at 60 months old.
   b) Among children not infected with HIV: there is no decline with age (i.e., 85% if vaccinated at the age of 9 months).
4. The proportions who are assumed to develop protective antibody titres after measles vaccination during SIAs are given below.
   a) Among HIV-infected children: 20% of those vaccinated at 13–24 months of age develop protective titres, 10% of those vaccinated at 25–36 months, 0% of those vaccinated at 37–48 months, and 0% of those vaccinated at 49–<60 months of age.
   b) Among children not infected with HIV: 95% of susceptible children if vaccinated when older than 12 months develop protective titres.
5. HIV-infected children who do not develop protective antibody titres after initial measles vaccination will not develop protective titres after revaccination.
6. Assumptions about the duration of passively acquired maternal antibodies are given below.
   a) For HIV-infected children: these are assumed to persist for 3 months.
   b) For children not infected with HIV: these are assumed to persist for 6 months.
7. Mortality rates used are shown in Table 1.
   a) For HIV-infected children data were extrapolated from published data (see text).
   b) For children not infected with HIV data were extrapolated from UNICEF statistics for infants and children less than 5 years old (Table 1).
8. Immunity to measles is maintained in HIV-infected adolescents and adults because measles immunity is acquired prior to HIV infection.

We calculated the percentage of children less than 5 years old who were immune to measles as a result of receiving routine measles vaccination at 9 months of age and routine vaccination combined with vaccination through mass campaigns or supplemental immunization activities (SIAs) (i.e., vaccination of children aged 9 months to 4 years). We evaluated a range of levels for routine measles vaccination coverage including 50%, 80% and 90%. For SIAs, we assumed coverage of 90%, which is the minimal rate considered to be effective (*2*). SIAs may provide equal coverage to both previously vaccinated children and unvaccinated children as campaigns that are independent of routine coverage, or they may first reach only those children previously vaccinated through routine service as campaigns that are dependent on routine coverage; rates of measles immunity were estimated for both situations. Calculations were performed using Excel software.

Prevalence of HIV infection in children

In sub-Saharan Africa, approximately 9% of women of childbearing age are infected with HIV, and in some regions the

Table 1. **Estimated proportion of HIV-infected children and HIV-uninfected children of different age groups in a hypothetical population under different mortality assumptions.** In this model 9% of children are assumed to be vertically infected with HIV, a figure corresponding to an HIV prevalence of 30% in adults. Thus, in a birth cohort of 100, 9 children will be infected with HIV and 91 will not be infected

Age group	HIV-uninfected children[a]		HIV-infected children					
			Low mortality		Middle mortality		High mortality	
	CM[b]	No./100 births	CM	No./100 births[c]	CM	No./100 births[c]	CM	No./100 births
0–12 months	10.8	81	20	7.2 (8.1)	33	6.0 (6.9)	40	5.4 (6.2)
13–24 months	13.5	79	30	6.3 (7.4)	40	5.4 (6.4)	50	4.5 (5.4)
25–36 months	15.5	77	40	5.4 (6.6)	66	3.1 (3.8)	75	2.3 (2.8)
37–48 months	16.5	76	45	5.0 (6.1)	70	2.7 (3.4)	85	1.4 (1.7)
49–60 months	17.5	75	50	4.5 (5.7)	75	2.3 (2.9)	90	0.9 (1.2)

[a] Based on UNICEF mortality rates for infants less than 1 year old and children less than 5 years old in sub-Saharan Africa. These rates include children infected with HIV and, thus, overestimate mortality for children not infected with HIV. Data were extrapolated for children aged 13–48 months.
[b] CM = cumulative mortality. Cumulative mortality is given as a percentage.
[c] Figures in parentheses are the percentage of all children in age stratum who are infected with HIV.

percentage is as high as 20–40% (*10*, *16–20*). Mother-to-child transmission of HIV is estimated to occur in about 30% (range = 25–48%) of infants born to HIV-infected mothers in Africa (*21–26*). Thus, in regions of high HIV prevalence, approximately 9% of infants will be infected with HIV, assuming a 30% prevalence of maternal HIV infection and a 30% rate of mother-to-child transmission.

Mortality of HIV-infected children in Africa

Mortality rates for HIV-infected children in sub-Saharan Africa vary by country and method of reporting (*22*, *27–33*). Two studies from Malawi and Kenya reported mortality of 35% and 43%, respectively, in HIV-infected children at 2 years of age (*27*, *34*), while studies in Malawi and Uganda reported mortality of 89% and 66%, respectively in HIV-infected children at 3 years of age (*31*, *34*). In a recent review, the mortality of HIV-infected children was estimated to be 26–45% at 1 year of age and 35–59% at 2 years of age (*35*). Reported mortality from studies probably underestimates true mortality because the provision of health care in the context of investigations is likely to be superior to that provided by routine health services; among children not infected with HIV, mortality rates reported by UNICEF are higher than those among the uninfected children followed in these study cohorts (Table 1). In Malawi, after the onset of AIDS-related symptoms, the median survival time among children was less than 10 months (*34*). HIV-infected children in sub-Saharan Africa are only rarely reported to survive to older childhood and adulthood.

Mode and timing of HIV transmission

Infants who acquire HIV infection in utero or at the time of delivery are more likely to be immunocompromised at a younger age and to die sooner than children who acquire HIV infection through breastfeeding. Two-year mortality rates among Kenyan children infected with HIV during the first 2 months of life were significantly higher than for children infected after the age of 2 months (63% versus 8.8%) (*27*). However, no studies have examined whether response to measles vaccination is affected by how the child's HIV infection was acquired (perinatally versus by breastfeeding). Therefore, distinctions between these two modes of transmission cannot be made for the purpose of estimating population immunity to measles.

Loss of protective maternal antibodies in infants born to HIV-infected women

Infants born to HIV-infected women may have lower levels of protective maternal antibodies independent of their own HIV infection status and may thus become susceptible to measles at a younger age, although this has not been consistently observed (*7*). The potential impact on measles control and elimination of a more rapid loss of protective maternal antibodies in infants born to HIV-infected women is unclear, but the risk of exposure to measles is low in early infancy in regions where measles has been successfully controlled in older children.

Response to measles vaccine

Limited data, mostly from the United States, show that people infected with HIV have lower response rates after vaccination and more rapid waning of antibody titres (*36–40*). While antibody titres are not synonymous with protection, they provide a good surrogate for measuring protective immunity and suggest that HIV-infected children are likely to have higher rates of both primary and secondary vaccine failure (*36–40*). In two prospective studies, only 25–37% of children developed measles-specific antibodies after vaccination at a mean of 23 or 81 months of age (*41*, *42*). However, younger children are less immunocompromised and may be more likely to develop protective antibody titres following measles vaccination.

In Zaire, 65% of children who were HIV-seropositive and vaccinated against measles at the age of 9 months had protective measles antibody titres at 1 year of age; however only 36% (4/11) of children with symptoms of HIV/AIDS seroconverted to measles compared with 77% (20/26) of children without symptoms of HIV/AIDS (*38*). In Thailand, 57% (9/16) of HIV-infected children vaccinated at 9 months of age had protective antibody titres 12 weeks after vaccination compared with 100% of 14 children without HIV who had been born to HIV-infected women (*43*). HIV-infected children in whom detectable antibodies fail to develop after initial measles vaccination often do not develop these antibodies following subsequent measles vaccinations; response rates in small studies of such cases range from 0–66% (*37*, *40*, *42*, *44*, *45*).

Few studies have examined the loss of measles antibodies after vaccination (as a surrogate measure for secondary vaccine failure) in children infected with HIV, although the median time to loss of measles-specific antibodies was 30 months in

Table 2. **Estimated proportion of HIV-infected children and HIV-uninfected children with measles immunity following routine and supplemental measles immunization.** See text for assumptions and estimates used in deriving the rates and for definitions of independent and dependent supplementary immunization activities (SIAs)

Age group (months)	90% routine coverage[a]		90% routine coverage plus 90% coverage in SIA[a]			
			Independent campaign		Dependent campaign	
	HIV-uninfected	HIV-infected	HIV-uninfected	HIV-infected	HIV-uninfected	HIV-infected
0–12	69.1	39.6	73.6	41.1	72.0	39.6
13–24	76.5	45.0	96.6	46.8	89.3	45.0
25–36	76.5	27.0	96.6	27.9	89.3	27.0
37–48	76.5	18.0	96.6	18.0	89.3	18.0
49–60	76.5	18.0	96.6	18.0	89.3	18.0

[a] Values are percentages of children with measles immunity.

one study (*39*). Interpretation of seroprevalence rates in cross-sectional studies is hampered by methodological differences, including age at vaccination, time of testing since vaccination, type of antibody assay, degree of immunosuppression at vaccination, and failure to exclude children with immunity due to infection with wild-type measles virus. Loss of antibodies among immunized children could account for the low seropositivity rates in some cross-sectional studies in the United States (*36*, *39–42*, *46*, *47*).

Measles immunity in HIV-infected adolescents and adults

The impact of HIV infection on susceptibility to measles depends on the timing of acquisition of the infection in relation to the development of measles immunity. Data from the United States suggest that immunity to measles is usually maintained if exposure to wild-type or vaccine-measles virus preceded HIV infection (*7*). Preliminary data from Malawi suggest that measles immunity following natural measles infection may persist in HIV-infected adults in developing countries as well (University of Malawi and Centers for Disease Control and Prevention, unpublished data, 2004). Thus, there is no evidence that susceptibility to measles increases in these adult populations, and loss of population immunity in older children and adults is not addressed in the model.

Findings

Box 1 shows the eight assumptions that were made in estimating the impact of the HIV pandemic on population immunity to measles in children. (Details of the calculations are available in Appendix 1 and Table 2.) The percentage of children less than 5 years old with immunity to measles resulting from routine measles vaccination was estimated in two hypothetical populations: one in which 30% of adults were infected with HIV and 9% of children were infected with HIV at birth, and one in which no adults or children were infected with HIV (Table 3). With this model, the differences in the percentage of children immune to measles between the hypothetical populations with and without HIV infection ranged from 1% to 2% in the different age strata (Table 3). When SIAs were added to the model (i.e., routine measles vaccination plus vaccination during SIAs) there was, as expected, a large increase in the percentage of children immune to measles in both hypothetical populations (Table 4). In addition, the difference between the percentage of children who were immune in the hypothetical population with HIV and that without HIV increased, ranging from 2.2% to 3.3%. Thus, under the initial assumptions, the HIV pandemic was estimated to decrease the percentage of children less than 5 years old who were immune to measles by approximately 2–3% per birth cohort.

Table 3. **Estimated percentage of children immune to measles in hypothetical populations with and without HIV infection by different coverage rates for routine vaccination.** See text for assumptions and estimates used in deriving the figures

Age group (months)	Coverage rate for routine vaccination								
	50%			80%			90%		
	% immune in population with HIV[a, b]	% immune in population without HIV	Difference	% immune in population with HIV[a]	% immune in population without HIV	Difference	% immune in population with HIV[a]	% immune in population without HIV	Difference
0–12	58.7	60.6	1.9	65.0	67.0	2.0	67.1	69.1	2.0
13–24	41.4	42.5	1.1	66.5	68.0	1.5	74.5	76.5	2.0
25–36	41.5	42.5	1.0	66.3	68.0	1.7	74.6	76.5	1.9
37–48	41.4	42.5	1.1	66.2	68.0	1.8	74.5	76.5	2.0
49–60	41.6	42.5	0.9	66.5	68.0	1.5	74.8	76.5	1.7

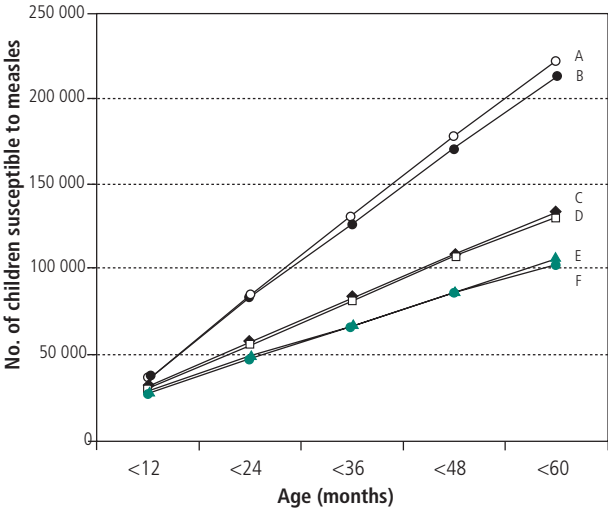
[a] Altogether 9% of children are assumed to be vertically infected with HIV, corresponding to an HIV prevalence of 30% in adults.
[b] All figures are percentages.

Table 4. **Estimated proportion of children immune to measles in hypothetical populations with and without HIV infection, by different coverage rates for routine vaccination and different strategies for supplemental immunization activities (SIAs).** See text for assumptions and estimates used in deriving the numbers and for definitions of independent and dependent SIAs

Age group (months)	Population					
	% measles immune, independent SIAs			% measles immune, dependent SIAs		
	HIV[a]	Without HIV	Difference	HIV[a]	Without HIV	Difference
	50% routine coverage, 90% SIA coverage					
0–12	69.5	71.6	2.2	68.6	70.7	2.2
13–24	88.0	91.7	3.7	84.1	87.6	3.5
25–36	88.9	91.7	2.8	85.0	87.6	2.6
37–48	88.9	91.7	2.8	85.0	87.6	2.7
49–60	89.3	91.7	2.4	85.4	87.6	2.3
	80% routine coverage, 90% SIA coverage					
0–12	70.9	73.1	2.2	69.5	71.7	2.2
13–24	92.0	95.4	3.3	85.9	88.9	3.0
25–36	92.7	95.4	2.7	86.5	88.9	2.4
37–48	92.6	95.4	2.7	86.4	88.9	2.5
49–60	93.1	95.4	2.3	86.8	88.9	2.1
	90% routine coverage, 90% SIA coverage					
0–12	71.4	73.6	2.3	69.8	72.0	2.2
13–24	93.4	96.9	3.2	86.5	89.3	2.8
25–36	94.0	96.6	2.6	86.9	89.3	2.4
37–48	93.9	96.6	2.7	86.9	89.3	2.4
49–60	94.3	96.6	2.3	87.2	89.3	2.1

[a] Altogether 9% of children are assumed to be vertically infected with HIV, corresponding to an HIV prevalence of 30% in adults.

Fig. 1. **Cumulative number of children susceptible to measles over five birth cohorts (0–60 months), assuming different rates of routine vaccination coverage. Calculations were based on an annual birth cohort of 100 000. In this cohort 65% of HIV-infected children were assumed to develop immunity to measles at 9 months of age.** The "middle mortality assumption" was used for HIV-infected children (see text and Table 1)



	% HIV-infected at birth	% coverage with routine measles vaccination
A	9	50
B	0	50
C	9	80
D	0	80
E	9	90
F	0	90

WHO 05.14

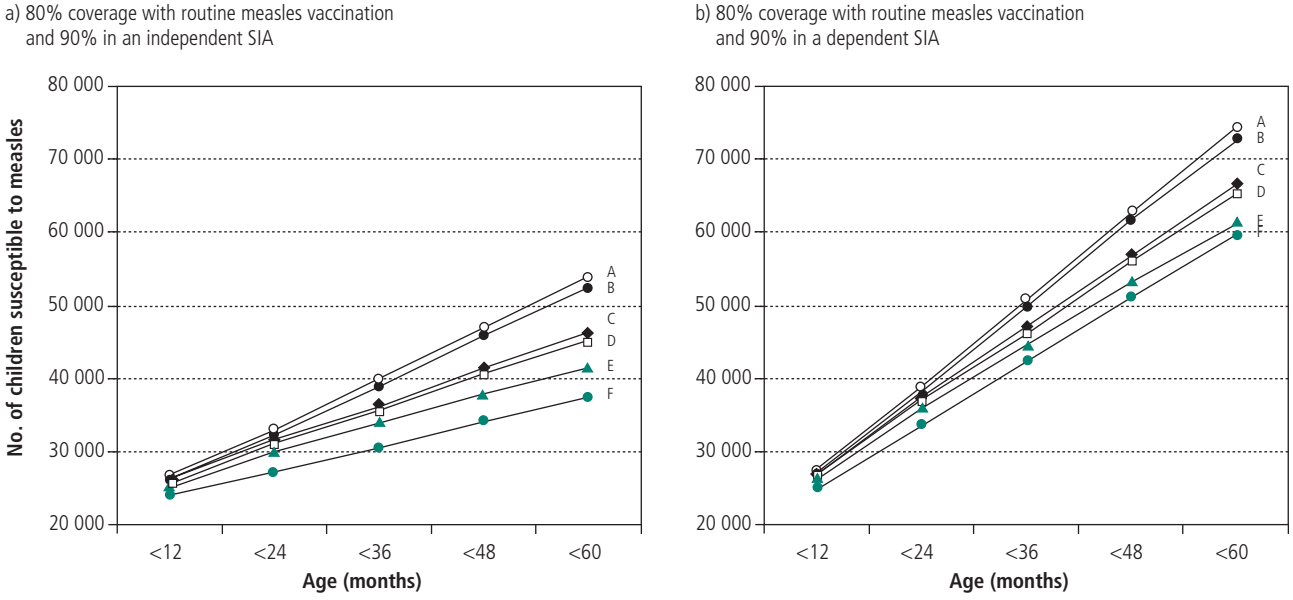
To illustrate the cumulative effect of a small decrease in population immunity to measles, the accumulation of measles-susceptible children over five birth cohorts was estimated, assuming an annual birth cohort of 100 000. Fig. 1 shows the accumulation of susceptible children at different rates of coverage with routine measles vaccination in the hypothetical populations with and without HIV infection. Fig. 2a) shows that with 80% coverage of routine vaccination and 90% coverage in an independent SIA campaign the cumulative number of measles-susceptible children less than 5 years old in middle-mortality populations with HIV (cohort D) and without HIV (cohort F) would be 45 390 and 37 370, respectively. Thus, there is a 21% relative increase in the number of susceptible children less than 5 years old. Fig. 2b) demonstrates the effect of a dependent SIA campaign.

Sensitivity analyses were performed by assuming that only 45% of HIV-infected children responded to vaccination at 9 months of age (Fig. 2) and the percentage protected at 24 months of age was 45%, at 36 months was 20%, at 48 months was 20% and at 60 months was 10%. Differences in the proportion of children immune to measles in the hypothetical populations with and without HIV-infected children increased from 2–3% to approximately 4–5% per birth cohort if measles vaccine seroconversion rates were reduced from 65% to 45% and the median survival of HIV-infected children was increased to 5 years (data not shown). Alternative scenarios were explored using low mortality rates and high mortality rates for HIV-infected children (i.e., median survival of 5 years and 2 years, respectively) (Fig. 2). An alternative scenario was also explored using the assumption that all infants born to HIV-infected mothers (i.e., 30% of infants) lost maternal antibodies at 3 months of age independent of the child's HIV status (data not shown). Using this assumption, the percentage of children less than 1 year old who were susceptible to measles increased by an additional 5% for the populations with HIV-infected children.

Discussion

Our model supports the experience of southern Africa, demonstrating that the impact of the HIV pandemic on measles population-immunity should not introduce an insurmountable barrier to measles control and elimination. This is partially because the impact of increased primary and secondary vaccine failure among HIV-infected children is counteracted by the high mortality rate of these children. For children aged 1–4 years, the HIV pandemic could result in a 2–3% increase in the portion of the birth cohort susceptible to measles, and this increase is greater when HIV-infected children survive longer. These models suggest that more frequent SIAs may be necessary to adequately control or eliminate measles in regions of

Fig. 2. **Cumulative number of children susceptible to measles over five birth cohorts (0–60 months) after both routine and supplemental measles immunization activities (SIAs), assuming different rates of seroconversion and mortality.**
Calculations were based on an annual birth cohort of 100 000. See text, Box 1 and Table 1 for details on mortality assumptions and seroconversion rates for children older than 9 months of age



	% HIV-infected at birth	% HIV-infected children who seroconvert at 9 months	Mortality assumption for HIV-infected children
A	9	45	Low
B	9	65	Low
C	9	45	Middle
D	9	65	Middle
E	9	65	High
F	0	Not applicable	Not applicable

SIA = Supplemental measles immunization activities

WHO 05.13

high HIV prevalence, but the optimal interval between SIAs was influenced more by the coverage rate of routine measles vaccination than by HIV prevalence.

The most significant factor resulting in an increase in the number of susceptible children was the absence of a second opportunity for vaccination. In addition, the impact of the type of campaign (dependent or independent) was much more significant than the presence of HIV in the population, the response of HIV-infected children to vaccination or the median survival of HIV-infected children. With an annual birth cohort of 100 000, 90% coverage of routine vaccination with a vaccine that is 85% effective, and no second vaccination opportunity, approximately 100 000 susceptible children less than 5 years old will accumulate over a five-year period (Fig. 1). This number is reduced to 60 000 if a dependent campaign is conducted and further reduced to 37 000 if an independent campaign is conducted (Fig. 2).

Our estimates do not account for other mechanisms by which the HIV pandemic may impact on population immunity to measles virus in children, such as the differential effects of the mode and timing of HIV infection (e.g. peripartum and transmission through breast milk) on response to vaccination and survival or the differential uptake of vaccination by children born to HIV-infected mothers versus those born to uninfected mothers. The model also does not incorporate the geographical heterogeneity (e.g., cities versus rural areas) that could be expected with regard to measles incidence, HIV prevalence and the survival of HIV-infected children. The model evaluated the strategy of routine vaccination plus SIAs in populations with and without HIV and would need to be adjusted if alternative strategies (such as providing a second dose in the routine vaccination programme) were used. Finally, these estimates are most relevant to settings aiming at measles elimination; they do not evaluate fully the impact of the HIV pandemic in settings that have mortality reduction goals with continued transmission of measles virus.

More generally, this analysis does not explicitly address other impacts of the HIV pandemic on measles elimination and control, such as the potential for prolonged or enhanced shedding of wild-type measles virus by people infected with HIV (*48*), the possible increased severity of measles in people who are infected with HIV (possibly due to increased immune suppression, altered vitamin A levels and poor nutritional status), the potential increased risk of serious adverse events following measles vaccination in HIV-infected children, or the possibility that the absence of characteristic signs and symptoms of measles in immunosuppressed people could hamper case–finding and surveillance and lead to nosocomial transmission of measles. Finally, the economic and social disruption caused by the HIV pandemic could affect coverage of measles vaccination and make the implementation of measles-control strategies more difficult. To incorporate many of these variables, more formal

assessment of the impact of HIV on population immunity using dynamic mathematical models is planned.

Many questions remain including: what are the primary and secondary failure rates and the optimal age of measles vaccination in HIV-infected children? What is the degree of shedding and what is the duration of shedding of wild-type measles virus by people infected with HIV? What are the clinical and immunological effects of repeated vaccination with live measles virus in children infected with HIV? What is the role of HIV-infected adults in the sustained transmission of measles, especially as vaccination programmes mature and more adults have immunity that is derived from measles vaccine which may be less robust than immunity derived from wild-type infection?

The magnitude and extent of the HIV pandemic has not yet peaked, and projections of large increases in the number of HIV-infected people in China, India and Russia are of great concern for many reasons including the potential impact on measles control. Finally, the impact of the widespread use of antiretroviral therapy on measles control strategies in sub-Saharan Africa will need evaluation. With the scaling-up of antiretroviral therapy in the region, more HIV-infected people will have access to treatment. Perinatal use of antiretroviral therapy will reduce the percentage of HIV infections acquired perinatally. Highly active antiretroviral therapy will improve the serological response to a second dose of measles vaccine (*49*, *50*) and may increase the median age of survival of children infected with HIV. While the early experience in southern Africa is encouraging, continued reanalysis of the epidemiology of measles and of the HIV pandemic will be critical in evaluating the optimal strategies for measles control in Africa and the rest of the world. ■

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Résumé

Évaluation de l'impact de la pandémie de VIH/Sida sur la lutte contre la rougeole et l'élimination de cette maladie

Objectif Évaluer l'impact de la pandémie de VIH/Sida sur l'immunité de la population vis-à-vis du virus rougeoleux acquise grâce au vaccin. La suppression de la transmission du virus de la rougeole dans des zones géographiques étendues exige des niveaux d'immunité élevés dans la population et l'infection à VIH peut réduire l'efficacité de la vaccination antirougeoleuse.

Méthodes Les auteurs ont réalisé une revue de la littérature pour évaluer les principaux paramètres conditionnant l'impact potentiel de l'infection à VIH sur l'épidémiologie de la rougeole en Afrique sub-saharienne. Ces paramètres comprenaient la prévalence du VIH, la mortalité infantile, les taux de transmission périnatale du VIH et les réponses immunitaires protectrices à la vaccination antirougeoleuse. Les auteurs ont introduit les estimations de ces paramètres dans un modèle simple, applicable à des régions où le VIH est fortement prévalent, pour évaluer l'impact potentiel de l'infection à VIH sur l'immunité de la population vis-à-vis de la rougeole.

Résultats Le modèle laisse à penser que la pandémie de VIH/Sida ne devrait pas opposer un obstacle insurmontable à la lutte contre la rougeole et à son élimination, du fait, en partie, de la compensation des taux plus élevés d'échec vaccinal primaire et secondaire chez les enfants séropositifs par le taux de mortalité plus important de ces enfants. La pandémie de VIH/Sida serait susceptible d'entraîner une augmentation de 2 à 3 % de la proportion de la cohorte de naissance vulnérable à la rougeole et des activités de vaccination supplémentaire plus fréquentes pourraient être nécessaires pour lutter contre cette maladie ou l'éliminer. D'après le modèle, le facteur influant le plus fortement sur l'intervalle optimal entre les activités de vaccination supplémentaire serait le taux de couverture par la vaccination antirougeoleuse systématique. Ce serait l'absence d'une deuxième chance de vaccination qui entraînerait la plus forte augmentation du nombre d'enfants vulnérables.

Conclusion Ces résultats contribuent à expliquer le succès initial des efforts d'élimination de la rougeole en Afrique australe, où l'on est parvenu à circonvenir la rougeole dans un contexte de forte prévalence du VIH.

Resumen

Evaluación del impacto de la pandemia de VIH en el control y eliminación del sarampión

Objetivo Estimar el impacto de la pandemia de VIH en la inmunidad poblacional de origen vacunal frente al virus del sarampión. Si se desea eliminar la transmisión del virus del sarampión en amplias zonas geográficas, es necesario garantizar un alto nivel de inmunidad en la población, pero la infección por VIH puede reducir la eficacia de la vacunación antisarampionosa.

Métodos Se llevó a cabo una revisión de la literatura para determinar los parámetros clave del impacto potencial de la infección por VIH en la epidemiología del sarampión en el África subsahariana; dichos parámetros fueron la prevalencia del VIH, la mortalidad en la niñez, las tasas de transmisión perinatal del VIH y la respuesta inmunitaria protectora a la vacunación antisarampionosa. Las estimaciones de esos parámetros se incorporaron en un modelo sencillo, aplicable a las regiones con alta prevalencia del VIH, para calcular el impacto potencial de la infección por dicho virus en la inmunidad poblacional contra el sarampión.

Resultados El modelo indica que la pandemia de VIH no tiene por qué suponer un obstáculo insuperable para el control y la eliminación del sarampión; ello se debe en parte a que las mayores tasas de ineficacia primaria y secundaria de la vacuna entre los niños infectados por el VIH se ven contrarrestadas por su alta tasa de mortalidad. La pandemia de VIH podría ocasionar un aumento del 2%-3% de la proporción de la cohorte de nacimiento vulnerable al sarampión, y tal vez se necesitarían actividades suplementarias de inmunización más frecuentes (ASI) para lograr controlar o eliminar esta enfermedad. En el modelo desarrollado,

el intervalo óptimo entre ASI dependía sobre todo de la tasa de cobertura de la vacunación antisarampionosa sistemática. La falta de una segunda oportunidad de vacunación es el factor que más incrementaba el número de niños vulnerables.

Conclusión Estos resultados ayudan a explicar el éxito inicial de los esfuerzos de eliminación del sarampión en el África austral, donde se ha conseguido controlar el sarampión en un entorno de alta prevalencia de la infección por VIH.

ملخص

تقيـــيم أثر جائحة الإيدز على مكافحة الحصبة والتخلُّص منها

الهدف: تقيـــيم أثر جائحة الإيدز على المناعة المكتسبة بالتطعيم لدى السكان تجاه فيروس الحصبة. فلابد من توافُر مستوى مرتفع من المناعة للتخلُّص من سراية فيروس الحصبة في المناطق الجغرافية الواسعة، كما أن العدوى بالإيدز قد تنقص من نجاعة التطعيم بلقاح الحصبة.

الطريقة: تمت مراجعة النشريات لتقيـــيم المتثابتات الرئيسة المتعلقة بالتأثير المحتمل للعدوى بالإيدز على وبائيات الحصبة في المناطق الواقعة جنوب الصحراء الأفريقية، وقد شملت المتثابتات معدلات انتشار الإيدز، ومعدلات وفيات الأطفال، ومعدلات سراية الإيدز في الفترة المحيطة بالولادة، والاستجابات المناعية الوقائية للتطعيم ضد الحصبة. وقد أدرجت هذه المتثابتات وتقديراتها في نموذج بسيط، يسهل تطبيقه على المناطق التي تعاني من معدلات مرتفعة من الإيدز، وذلك لتقيـــيم التأثير المحتمل للعدوى بالإيدز على مناعة السكان تجاه الحصبة.

الموجودات: يوضّح النموذج أن جائحة الإيدز ينبغي ألا تدخل عائقاً يحول دون مكافحة الحصبة والتخلُّص منها، والسبب في ذلك يعود جزئياً إلى المعدلات المرتفعة للفشل الأولي والثانوي للقاح الحصبة لدى الأطفال المصابين بعدوى الإيدز، وما يقابله من معدلات مرتفعة للوفيات بينهم. وقد تؤدي جائحة الإيدز إلى ازدياد مقداره 2 –3 بالمئة في نسبة المواليد الأتراب المستعدين للإصابة بالحصبة وتتطلب المزيد من أنشطة التمنيع التكميلي المتكرِّر، فذلك قد يكون ضرورياً للتخلُّص من الحصبة. ووفقاً لهذا النموذج فإن الفترات الفاصلة بين أنشطة التمنيع التكميلي تتأثر أكثر ما تتأثر بمعدلات التغطية بالتطعيم ضد الحصبة. إن غياب فرصة ثانية للتطعيم يؤدي إلى ازدياد كبير في عدد الأطفال المستعدين للإصابة بها.

الاستنتاج: تساعد هذه النتائج على تفسير النجاح المبدئي لجهود التخلُّص من الحصبة في جنوب أفريقيا، حيث أمكن مكافحة الحصبة في موقع يعاني من معدلات عالية لانتشار الإيدز .

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Appendix 1

The estimates of immunity to measles in the population with HIV-infected children were derived by multiplying the proportion of HIV-infected children immune to measles by the proportion of HIV-infected children in an age-specific stratum. This was then added to the proportion of HIV-uninfected children immune to measles multiplied by the proportion of HIV-uninfected children in the age stratum. Thus, for children aged 0–12 months and with 90% coverage of measles vaccination, the proportion of children immune to measles is the proportion of HIV-infected children immune to measles (39.6%, from Table 2) multiplied by the proportion of HIV-infected children in the age-specific stratum (6.9%, from Table 1 "middle mortality") plus the proportion of HIV-uninfected children immune to measles (69.1%, from Table 2) multiplied by the proportion of HIV-uninfected children in the age stratum (93.1%, which is 1.000–0.069). Thus, (0.396 x 0.069) + (0.691 x 0.931) = 0.671.

To demonstrate how the estimates in Table 2 were derived, consider the measles immunity rates for HIV-uninfected children with routine coverage only. For children in the age strata that represent those older than 12 months, the estimates are straightforward: 85% seroconversion multiplied by 90% coverage. For children less than 12 months old, the calculation includes the assumption that children less than 6 months old have protective maternal antibodies and only children 9–12 months of age are vaccinated. The simplifying assumption was made that 100% of infants were protected by maternal antibodies to the age of 6 months, with none being protected after that age, although maternal antibody decay begins soon after birth, with a resultant exponential fall in the proportion of children protected over the first year of life. Thus, 0.5 + (0.25 x 0.85 x 0.9) = 0.69. Supplemental immunization activities add an additional number of immune children. For children aged > 12 months who then participate in an independent SIA, the proportion of those who are immune increases by the percentage of non-immune children (23.5%) multiplied by the 95% seroconversion rate and 90% coverage rate, so 0.235 x 0.95 x 0.9 = 0.2009. For a dependent campaign, the proportion of "eligible" children decreases from 23.5% to 13.5% (0.135 x 0.95= 0.128) because the 10% missed by routine coverage are not reached in the SIA.

The calculations for children infected with HIV are similar except that maternal antibodies persist for only 3 months; only 65% of children seroconvert at 9 months of age; the proportion of children immune decreases with age; previously vaccinated but non-immune children are assumed not to respond to a second dose of measles vaccine; and age-specific seroconversion rates are used for the SIA. Under these assumptions, independent SIAs had little effect on the proportion of HIV-infected children who were immune to measles (Table 2).