Update/Le point

Principles of measles control*

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WHO's Expanded Programme on Immunization has significantly helped to reduce global morbidity and mortality from measles. Recently, some African countries with high vaccine coverage levels have reported measles outbreaks in children above the current target age group for immunization. Outbreaks such as these are to be expected, unless close to 100% of the population are immunized with a vaccine which is 100% effective. Success of an immunization programme requires identification of the distribution and ages of susceptible children and reduction of their concentration throughout the community. Priority should be given to urban and densely populated rural areas. In large urban areas, high coverage of infants must be achieved soon after the age at which they lose their maternal antibodies and become susceptible. This will be facilitated by the introduction of high-dose measles vaccines which can be given at 6 months of age. Where measles incidence is increasing among children aged over 2 years, immunization of older children may be considered during contacts with the health care system, or at primary school entry, if this does not divert resources from immunization of younger children. Health workers should be informed of the predicted changes in measles epidemiology following immunization. The collection, analysis and use of data on measles (vaccine coverage, morbidity and mortality) should be improved at all levels of the health care system in order to monitor the immunization programme's overall impact, identify pockets of low coverage, and allow early detection of and response to measles outbreaks.

Introduction

The Expanded Programme on Immunization (EPI) currently prevents over 1.35 million deaths from measles in developing countries per year. Despite

the progress of the EPI, only 59% of children under one year of age were estimated to have received measles vaccine in 1988, and measles still causes an estimated 1.5 million deaths per year. Recently, some African countries with measles vaccine coverage of 70% or higher have reported outbreaks of measles, some of which affected children outside the current target age group for immunization. This has prompted a reexamination of the strategies for measles control.

This paper reviews the epidemiology of measles in the pre- and post-immunization eras, based on examples from Africa and the USA, and relates this to the effect of immunization programmes predicted by mathematical models. Recommendations are made for the improvement of measles control in developing countries. The paper does not describe additional strategies which may be considered by countries with measles elimination as the goal.

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Measles epidemiology in the pre-immunization era

In large unimmunized populations, measles incidence varies cyclically. An increase in the number of persons susceptible to infection or in the frequency of contact between infectious individuals and susceptibles leads to an increase in measles incidence. As incidence rises, the number of susceptible persons decreases; this reduces the chances of an infectious person making contact with a susceptible person and measles incidence begins to fall. As the incidence falls, susceptibles accumulate until a threshold is passed, at which time measles transmission increases again. The length of the inter-epidemic interval depends on the rate of accumulation of susceptibles, which is in turn dependent on population density, birth rate and migration patterns. In urban areas of Africa, epidemics occurred every 1–2 years in the pre-immunization era. Rural areas of Africa experienced sporadic localized outbreaks with intermittent spread to adjoining regions. In urban areas of the USA, epidemics occurred every 2–5 years prior to immunization (1).

In the absence of immunization, the age distribution of cases depends on the rate of maternal antibody loss and age-related changes in frequency of contact with other persons. Measles infects younger children more in developing than in developed countries, because of the earlier loss of maternal antibody and higher birth rates. Prior to immunization, the median age was 1.5–2.5 years in urban Africa, 2.5–5 years in rural Africa (2), and 4–9 years in urban and 6–10 years in rural areas of the USA (1).

Important foci of transmission in developing countries have been health centres, the homes of neighbours or relatives in other villages (3), and gatherings for festivals and markets. Infection is also passed on from endemic urban areas to rural areas. In developed countries, schools have been important places of contact, leading to relatively high incidence rates in school-age children (4).

Case-fatality ratios (CFR) in developing countries have varied in community studies from 3% to 15% (5, 6). CFRs are higher in young children, secondary cases (2), and malnourished children. The risk of delayed mortality is increased for children, especially when measles occurs before one year of age (7).

Effect of immunization on measles epidemiology

Mathematical models

Mathematical models have assisted in our understanding and prediction of changes in measles epidemiology which follow widespread immunization. Programmes that immunize a portion of the birth cohort each year slow down the rate of entry of new susceptibles into the population and hence decrease measles incidence. This leaves some children susceptible to infection till an older age, leading to a shift in the age distribution of measles towards older children and a lengthening of the inter-epidemic interval.

The period of low incidence following the introduction of widespread immunization, termed the "honeymoon period", is generated during the shift from the pre-immunization to the post-immunization age distribution of susceptibles (8). Rapid achievement of high coverage induces a period of low incidence, during which older persons are immune from exposure to the natural disease and younger persons are immune after immunization. As the cohorts grow older while the disease incidence is low, most persons acquire immunity from exposure to the vaccine rather than to the disease. If coverage is less than 100%, and the vaccine is less than 100% effective, the incidence will rise after a long disease-free or low-incidence period, though remaining lower than the pre-immunization level, with a longer inter-epidemic period. Thus, a dramatic short-term reduction in measles incidence after mass immunization may be followed by the recurrence of measles epidemics, at ever-increasing intervals.

Immunization programmes aim to interrupt measles transmission by inducing herd immunity, which is the resistance of a group to attack by measles since a large proportion of the members are immune, thus reducing the chance of contact between an infectious person and a susceptible individual. The high transmissibility of measles makes herd immunity difficult to achieve. Hope-Simpson estimated that 75.6% of household exposures of susceptibles lead to measles transmission, compared to 61% for varicella and only 31.1% for mumps (9). It has been estimated that around 95% immunization coverage with a vaccine which is 100% effective must be achieved to eliminate measles from a stable population. However, these estimates assumed that immunization occurred immediately after the waning of maternal antibody-mediated protection and was uniform throughout the population (10). If some pockets of the community contain a large enough number of susceptibles, among whom contacts are frequent, there may still be the potential for epidemics in these pockets despite such high overall coverage.

The change in age distribution of measles cases and the longer inter-epidemic period predicted by

mathematical models have been seen in countries with mature immunization programmes.

Experience in the USA

In the USA, measles immunization was introduced in 1963. The incidence fell rapidly (Fig. 1), and in 1978 a measles elimination initiative was announced. The age distribution of cases in the USA changed markedly after the immunization programme. In the pre-immunization period only 10% of cases were in persons over 10 years of age. In 1989, 54% of cases were over 10 years old (11).

Measles elimination proved more elusive than anticipated. Although the USA was close to elimination of indigenous measles in the early 1980s, the reported incidence in 1989 (provisional total, 17 850 cases) was the highest since 1978, and the reported deaths (provisional total, 41) was the highest since 1971. In 1989–90, the absolute and relative incidences among preschool-age children have increased, although the total reported incidence is still less than 5% of that in the pre-vaccine era (11).

The need to achieve uniformly high coverage at the appropriate age is demonstrated by the occurrence of measles outbreaks in the USA in unimmunized preschool-age children and among sectors of the community with religious exemptions to immunization (12). Although over 96% of schoolchildren are immunized because of the legal requirement for immunization before school entry, vaccine coverage at age 2 years is less than 50% in many areas. This susceptible pool of unimmunized preschool-age children sustains large epidemics in inner cities.

In contrast to preschool measles cases, which occur principally among unimmunized children, school outbreaks occur despite immunization coverage of over 98%, and transmission has been documented among persons who received the vaccine at an appropriate age (13). In a highly immunized population, a large proportion of cases is expected among immunized persons, since there are so few unimmunized persons. For example, if 98% of the population is immunized with a vaccine that is 95% effective, 71% of cases are predicted to occur among vaccinated persons (14). In the USA the overall attack rates in school outbreaks have been low (1–5%), and vaccine efficacy has been estimated as 95% or more.

In response to the resurgence of measles, the USA has launched an initiative to increase age-appropriate immunization coverage, targeted to inner-city areas, and has recommended a routine second dose of measles vaccine at school age, to protect the 2–5% of persons who did not respond to an initial dose of vaccine given at an appropriate age (15).

Fig. 1. **Reported measles cases in the USA, 1950–89.**
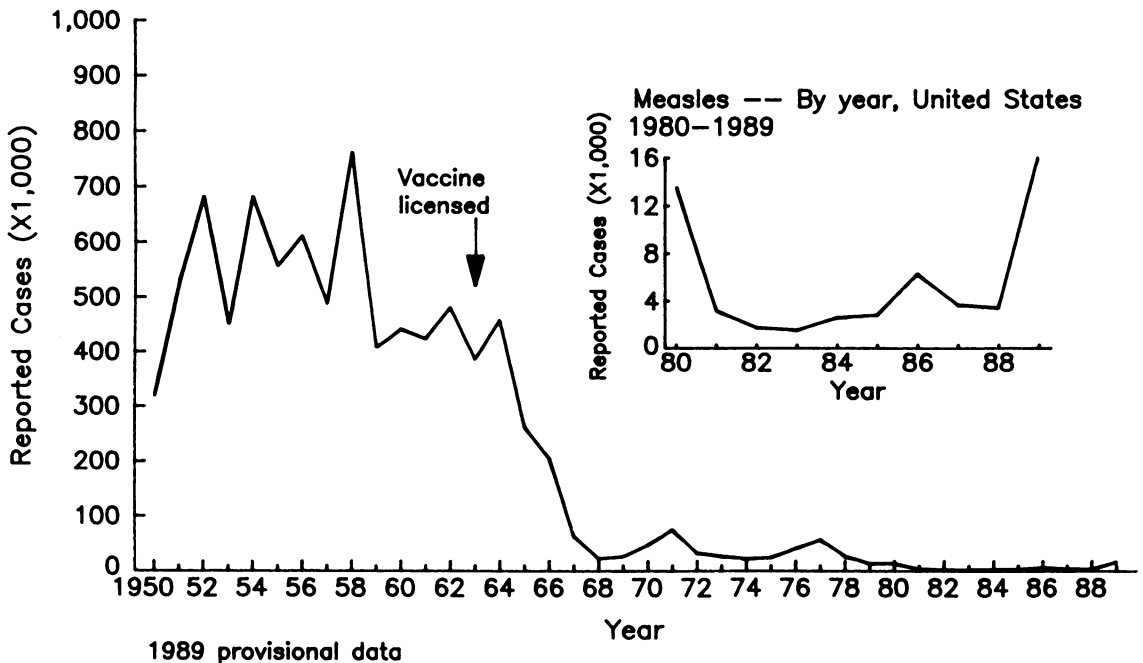
Experience in Africa

In Africa, measles immunization was first introduced during the smallpox eradication/measles control campaigns in the late 1960s. The campaigns dramatically reduced measles incidence, but rebounds in incidence quickly followed (1, 3). Measles immunization was subsequently integrated into routine health services. Average coverage in Africa increased from 16% in 1983 to 45% in 1988. In 1988, eight African countries reported coverage for measles vaccine in under-one year olds of over 75%.

One of the problems of measles immunization in developing countries is the early age of onset of measles. Based on serological and epidemiological studies in Kenya, WHO recommended a single dose of measles vaccine at 9 months of age. It was expected that increasing coverage in older children would decrease transmission to younger infants, as occurred in Yaounde, Cameroun (16). However, in other large cities, measles in children under 9 months old remains a major problem despite higher coverage rates (17), and has led to renewed interest in lowering the age for routine measles immunization.

A more recent problem in some countries that have achieved and sustained high coverage rates is an increase in the proportion of measles cases occurring in children over two years of age (above the target age group for immunization), and the occurrence of outbreaks in older children, after several years of low incidence (Table 1). In Lesotho and Swaziland, both small countries with dispersed populations, school outbreaks occurred in 1987–88, though the attack rates were low (5% in grades 1–3 in recent school outbreaks in Swaziland). [a,b]

In Burundi and Rwanda, countries with predominantly rural populations but high population density, recent outbreaks have occurred among both schoolchildren and preschool-age children. Most cases were reported to be among unimmunized children, although there was little documentation of immunization status among school-aged children. In Rwanda, most cases occurred among children over 5 years old, but case-fatality ratios were highest in under-two year olds (Table 2). [c]

[a] **Foster, S.O.** Options for measles control in Lesotho. International Health Program Office, Centers for Disease Control, Atlanta, GA, USA (unpublished report).

[b] **Simpson, D.** Foreign trip report, Swaziland, 1989. International Health Program Office, Centers for Disease Control, Atlanta, GA, USA (unpublished report).

[c] **Weierbach, R.** Rapport de mission au Rwanda du 21 juillet au 4 aout 1989. International Health Program Office, Centers for Disease Control, Atlanta, GA, USA (unpublished report).

Table 1: Measles epidemiology in selected countries with medium-to-high vaccine coverage in sub-Saharan Africa

Country	Vaccine coverage[a]	>50% since:[b]	% of reported cases in children ≥5 years
Burundi	57	1986	35
Lesotho	78	1982	62
Rwanda	86	1983	31
Swaziland	74	1986	41

[a] Vaccine coverage in children aged 12–23 months, measured in the most recent cluster survey, incuding history of immunization for children without documentation.
[b] Year since when measles vaccine coverage has been over 50%.

Table 2: Reported case-fatality ratios (CFR) in Byumba region, Rwanda, 1989

Age (months)	No. of cases	No. of deaths	CFR (%)
0–8	135 (9.2)[a]	4 (28.6)	3.0
9–23	210 (14.3)	3 (21.4)	1.4
24–59	279 (19.0)	3 (21.4)	1.0
≥60	846 (57.5)	4 (28.6)	0.5
Total	1470 (100.0)	14 (100.0)	1.0

[a] Figures in parentheses are percentages.

An investigation in one primary school in Burundi suggested that schoolchildren were an important source of infection for younger siblings. [d] Twenty-eight cases occurred among 299 students in grades 1–5 (attack rate 9%); 25 of them were the primary cases in their household, and gave rise to 31 secondary cases, 90% of which were in younger siblings.

Despite these outbreaks, overall measles morbidity and mortality have greatly declined in these countries (Fig. 2–4). In Burundi, the reported morbidity and mortality rates decreased by over 50% from 1981 to 1988. In Rwanda the reported incidence in 1988 was 3% of that in the pre-immunization period.

Because measles has a lower CFR in older children, the shift in age distribution from young to older children reduces overall measles mortality and is a positive result of the immunization programme.

[d] **Chen, R.T.** Foreign trip report, Burundi, 1989. International Health Program Office, Centers for Disease Control, Atlanta, GA, USA (unpublished report).

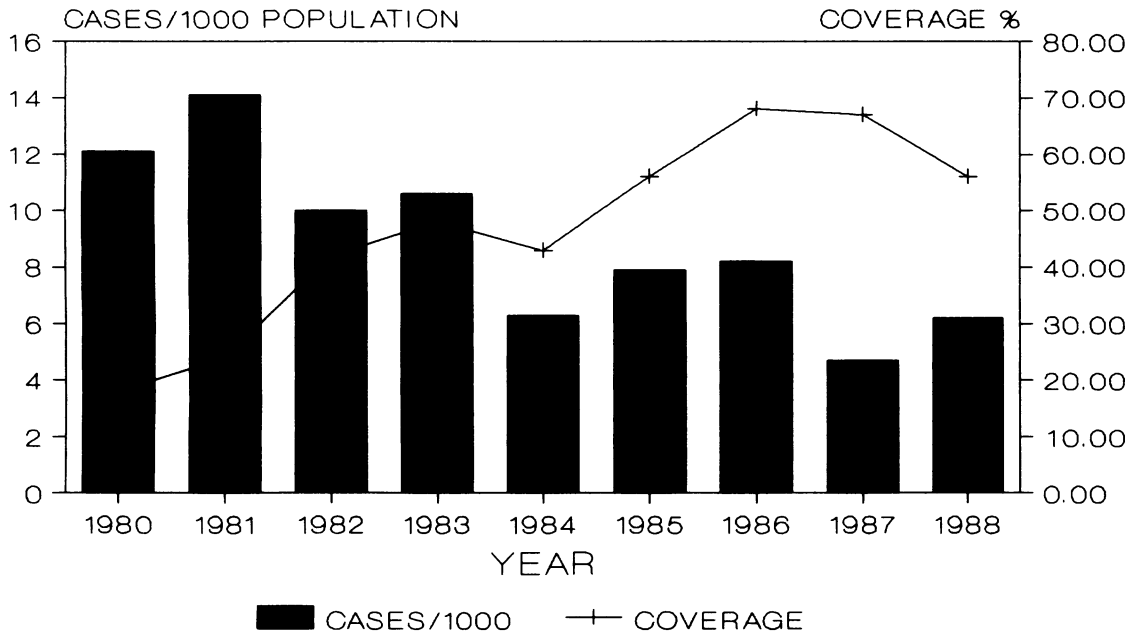Fig. 2. **Reported measles incidence and vaccine coverage in Burundi, 1980–88.**

Fig. 3. **Reported measles incidence and vaccine coverage in Lesotho, 1980–87.**
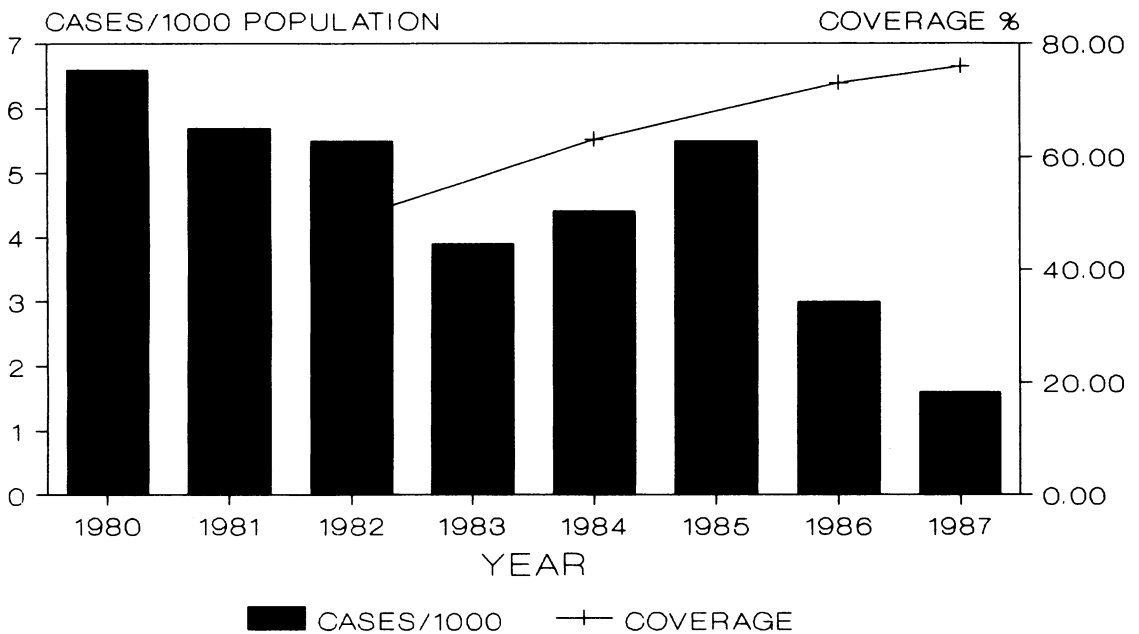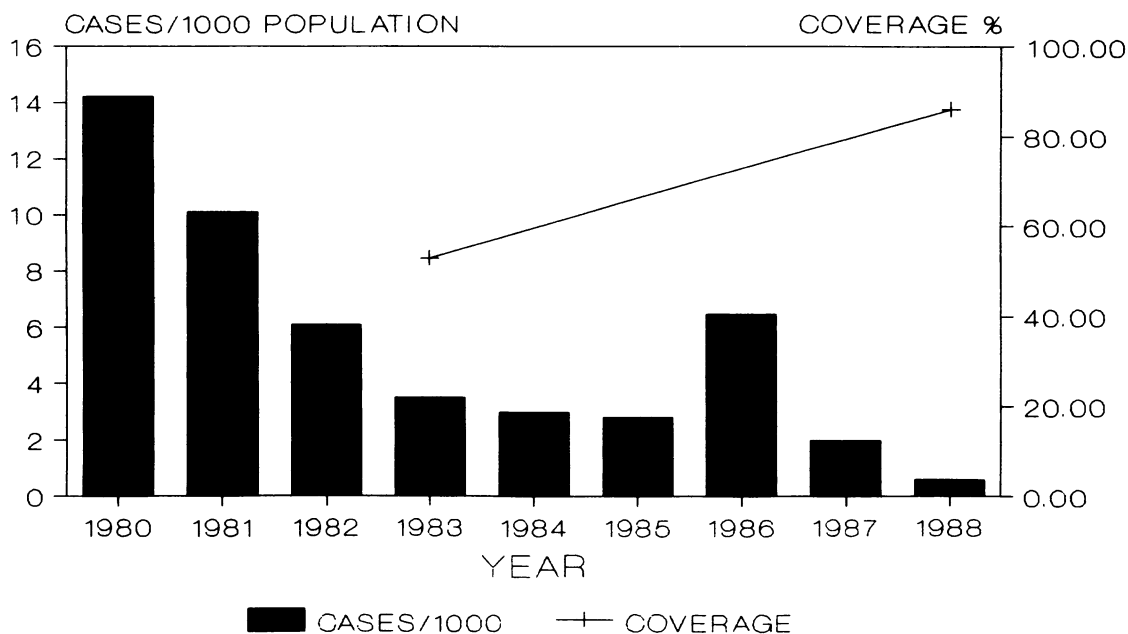
Fig. 4. **Reported measles incidence and vaccine coverage in Rwanda, 1980–88.**

However, outbreaks involving school-age children may lead to the infection of younger, more vulnerable children and be associated with high case fatality because of the high number of secondary cases. The high visibility of outbreaks occurring after the investment of substantial resources to raise coverage may lead to a loss of confidence in the immunization programme among health workers, the public and political leaders, and to the diversion of resources from routine immunization of infants. Health workers may also become discouraged if surveillance data fail to demonstrate the programme's impact. In countries with poorly developed surveillance prior to the immunization programme the reported measles cases may even increase as the programmes get stronger, because of increased completeness of reporting.

Discussion

The Expanded Programme on Immunization has made significant progress in reducing morbidity and mortality from measles. Although measles outbreaks have begun to occur in older children in some countries with high coverage, this is an expected consequence of an immunization programme whose target age group has been children under 2 years.

Another expected result of high coverage levels is an increase in the proportion (but not the rate) of cases among previously immunized children (14). The occurrence of either of these does not necessarily indicate programme failure. In the countries concerned, measles incidence and mortality rates have been substantially reduced.

To improve the immunization programmes further, the age and subgroup distribution of susceptibles should be determined and actions targeted to pockets of low coverage. The priority remains to attain and sustain high coverage as soon as possible after the age when most infants have lost maternal antibody and become susceptible. When measles incidence is increasing among children over two years of age, permissive immunization of older children may be considered during contacts with the health care system, or at primary school entry, if this does not divert resources from immunization of younger children.

Measles control in urban areas deserves priority to reduce mortality among young children and transmission to rural areas. Three essential actions to increase coverage are the avoidance of missed immunization opportunities, establishment of a system for detection and referral of defaulters from immunization, and the identification of pockets of low coverage.

Health workers should be informed of the predicted changes in measles epidemiology following immunization and of the importance of identifying and immunizing clusters of susceptible persons. The collection, analysis and use of data on vaccine coverage, measles morbidity and mortality should be improved at all levels of the health care system, to monitor the programme's overall impact, identify potential pockets of low coverage, and allow early detection of measles outbreaks. Programme managers should liaise with administrative authorities and with the media to provide feedback to political leaders and the public on the progress made by the EPI, and to enlist the cooperation of community leaders in detecting groups of susceptible persons.

The decision on when to respond to an outbreak depends on the previous incidence of measles in the area and the resources available. In special situations such as refugee camps, where the potential for rapid and widespread transmission is great, rapid response to any measles case is essential. In areas endemic for measles, there is no single definition of an outbreak. A working guide is that if the present number of cases exceeds that in the same period in previous non-epidemic years, then further investigation is warranted. Recommendations for outbreak investigation and control have been outlined previously and are not repeated here.[e]

Immunization programmes in developing countries are increasing coverage rapidly, with the result that measles epidemiology is constantly changing. Strategies for measles control need to evolve as the EPI gets strengthened. In large urban areas, the pool of children who have lost maternal antibodies but have not yet reached the minimum age for immunization contributes to sustaining measles transmission even at high coverage levels. Vaccines which can be applied at 6 months of age will assist in measles control in areas where measles before the age of 9 months is a significant cause of death (18).

Some European countries have achieved measles control through high coverage of preschool-age children and a two-dose schedule. The USA is currently introducing a routine two-dose schedule. Evaluation of the impact and cost of two-dose schedules, the serological response to the second dose, and operational research on the timing of the second dose will provide valuable information for other countries which may be considering measles elimination programmes in the future.

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[e] **Strassburg, M.A.** *Guidelines for the investigation and control of outbreaks of EPI target diseases.* Unpublished WHO document EPI/GEN/84/7, 1984.

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