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Measles control in the 1990s: Minimizing nosocomial transmission

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Contents

1. Introduction

In 1989, the World Health Assembly declared the goal of global measles control, defined as "the reduction in measles incidence of 90% from pre-immunization levels by 1995" (WHA, 1989).

In 1990, this goal was further refined by heads of state during the World Summit for Children to "the reduction by 95% in measles deaths and reduction by 90% in measles cases compared to pre-immunization levels by 1995, as a major step to the global eradication of measles in the longer run" (WHO, 1992).

The Global Programme for Vaccines (formerly comprised in part by the Expanded Programme on Immunization) of the World Health Organization (WHO) has recommended a series of strategies for achieving the measles control goals (WHO, 1993a). At country level, these strategies include achieving coverage of at least 90% of infants under one year of age with one dose of potent measles vaccine, the vaccination of other age-groups, as indicated through epidemiological analysis, the vaccination of high-risk groups, including children admitted to hospital, the elimination of missed opportunities for vaccination, and the systematic development and implementation of mass communication, epidemiological surveillance, outbreak response and improved clinical case management.

Measles is generally considered one of the most infectious human pathogens, and certainly the most contagious vaccine-preventable disease. This is due to the ability of the virus to remain airborne for extended periods in small-aerosolized droplets released by the patient upon coughing (Bloch, 1981; Langmuir, 1980; Remington, 1985).

Measles transmission is therefore facilitated by the collection of susceptible individuals in confined spaces where aerosolized droplets containing measles virus are not readily cleared from the air. Settings where susceptible persons congregate and risk exposure to infected persons constitute an ideal environment for measles transmission. Outside the home, high-risk settings include educational facilities, gymnasia, churches, orphanages, refugee camps and health facilities (Markowitz, 1989; Gindler, 1992).

Health facilities are of particular concern because of the enhanced risk of exposure to persons with measles who have been brought for diagnosis and treatment.

Cases of nosocomial measles are those which are acquired as a result of being infected in a health facility. The purpose of this paper is to review the recent literature, where possible to quantify the contribution of nosocomial transmission to overall measles incidence and to provide practical recommendations to national EPI programme managers on strategies to minimize opportunities for nosocomial transmission.

2. Epidemiology of nosocomial measles

An early study of nosocomial infection conducted in 1946-47 in 26 children's wards in 14 representative hospitals throughout the United Kingdom found that 12% of all nosocomial infections were due to measles (Watkins, 1949). A similar finding was reported among low socioeconomic class black children admitted to a major teaching hospital in South Africa in 1987 (Cotton, 1989). Both studies may have under-estimated the proportion of nosocomial infections due to measles since post-discharge surveillance was not performed in the former study, or limited to readmitted patients in the latter.

The relative contribution of nosocomial transmission to the overall incidence of measles appears to vary considerably, in accordance with the prevailing epidemiology of measles (Table 1).

Published national measles surveillance data are available from the USA during the decade of the 1980s, where high vaccination coverage reduced measles incidence to historically low levels and the great majority of reported cases were clustered in outbreaks (WHO, 1990). Data include information on the probable source of exposure for an average of half of reported cases.

Overall, less than 10% of cases with a reported probable source of exposure were infected in health facility settings during the period 1980-90, but nosocomial transmission, as a proportion of all exposures, increased 20-fold in roughly linear fashion during the period. Although these data are limited by the potential bias associated with the large proportion of cases with no reported source of exposure, it is unlikely that this would explain the increasing trend observed in the contribution of nosocomial spread.

Analysing data derived from measles outbreak investigations available from three industrialized countries (France, South Africa and USA), the proportion of cases with reported exposure in health facility settings ranged from 15% to 72%. The proportion of cases associated with nosocomial spread was reported to be generally lower in community-based studies (CDC, 1984; Dales, 1985; Istre, 1987) than in studies of specific urban health facility-based outbreaks or those restricted to hospitalized cases (Foulon, 1986; CDC, 1987; Reynolds, 1987; Sienko, 1987; McGrath, 1992; Mason, 1993). This finding is to be expected since facility-based studies tend to exaggerate the importance of community members who use health facilities with greater frequency and therefore tend to over-estimate the rate at which the event actually occurs in the community.

Case-control studies performed in Los Angeles and Houston showed that attendance at a hospital emergency room 10-18 days prior to rash onset was a significant risk factor for acquiring measles (Farizo, 1991).

Analysing data derived from measles outbreak investigations available from six developing countries (Brazil, Burundi, Cameroon, Côte d'Ivoire, Guinea-Bissau and Mozambique), the proportion of cases with reported exposure in health facility settings ranged from 21% to 71%. The proportion of cases associated with nosocomial spread was reported to be generally similar in a community-based study (PAHO, 1983) and in studies of specific urban health facility-based outbreaks or those restricted to hospitalized cases (Guyer, 1976; Rabelo; 1982; Aaby, 1985).

A case-control study performed in Abidjan also showed that attendance at a hospital emergency room during the measles incubation period was a significant risk factor for acquiring measles (WHO, 1986a; Klein-Zabban, 1987). However, a study in a rural area of Burundi found no difference in the proportion of cases and controls who had visited a health facility during the previous month (Chen, 1990). Furthermore, a separate community-based study found that only 1% of measles cases had visited a health facility during the previous month.

In summary, these studies demonstrate that nosocomial contact is an important mechanism of measles transmission in industrialized countries and in the urban setting in developing countries. Furthermore, evidence from the USA suggests that the relative contribution of nosocomial transmission to measles incidence may be expected to increase in the future as high vaccination coverage rates are achieved in more countries (WHO, 1993a) and where endemic (non-outbreak) measles declines substantially in importance.

However, the findings also suggest that transmission by the nosocomial route does not yet contribute significantly to measles incidence in rural communities in developing countries where vaccination coverage remains low moderate and where either access to health facilities or their utilization by community members for diseases like measles is limited.

Table 1(a). Relative contribution of nosocomial transmission to measles incidence in developed and developing countries (Industrialized countries)

Country	Year	Cases associated with nosocomial spread (%)	Reference
National surveillance			
USA	1980	0.4	CDC, 1981
"	1981	1.1	Davis, 1986
"	1982	1.2	"
"	1983	3.7	"
"	1984	2.5	"
"	1985	4.7	CDC, 1986
"	1987	6.2	CDC, 1988
"	1989-90	9.0	Gindler, 1992
Outbreak investigations:			
a) community-based			
USA (Oklahoma)	1981-85	27	Istre, 1987
USA (California)	1983	29	Dales, 1985
USA (Hawaii)	1984	15	CDC, 1984
b) facility-based			
France	1983-84	16	Foulon, 1986
USA (Michigan)	1985	57	Sienko, 1987
USA (New Mexico)	1986	43	CDC, 1987
South Africa	1985-86	25	Reynolds, 1987
USA (Michigan)	1990	48	McGrath, 1992
USA (California)	1990	72	Mason, 1993
c) case-control			
USA (California)	1988-89	23[1]	Farizo, 1991
USA (Texas)	1988-89	41[1]	Farizo, 1991

[1] Significantly more cases than controls had visited a health facility during the measles incubation period.

Table 1(a). Relative contribution of nosocomial transmission to measles incidence in developed and developing countries (Developing countries)

Country	Year	Cases associated with nosocomial spread (%)	Reference
Outbreak investigations:			
a) community-based			
Brazil	1983	21	PAHO, 1984
b) facility-based			
Cameroon	1975	35	Guyer, 1976
Mozambique	1980	33	Rabelo, 1982
Guinea-Bissau	1980-82	16	Aaby, 1985
c) case-control			
Côte d'Ivoire	1985	71[1]	Klein-Zabban, 1987
Burundi	1988	32[2]	Chen, 1990

[1] Significantly more cases than controls had visited a health facility during the measles incubation period.

[2] There was no significant difference in the proportion of cases and controls who had visited a health facility during the previous month. A separate community-based study found that only % of measles cases had visited a health facility during the previous month.

3. Factors influencing the control of nosocomial measles

3.1 Characteristics of transmission

Measles is an acute, highly contagious disease transmitted by direct contact with infectious droplets or, less commonly, by airborne spread (American Academy of Pediatrics, 1991). Immunity following disease is lifelong; seroconversion following successful immunization is also, for all practical purposes, lifelong.

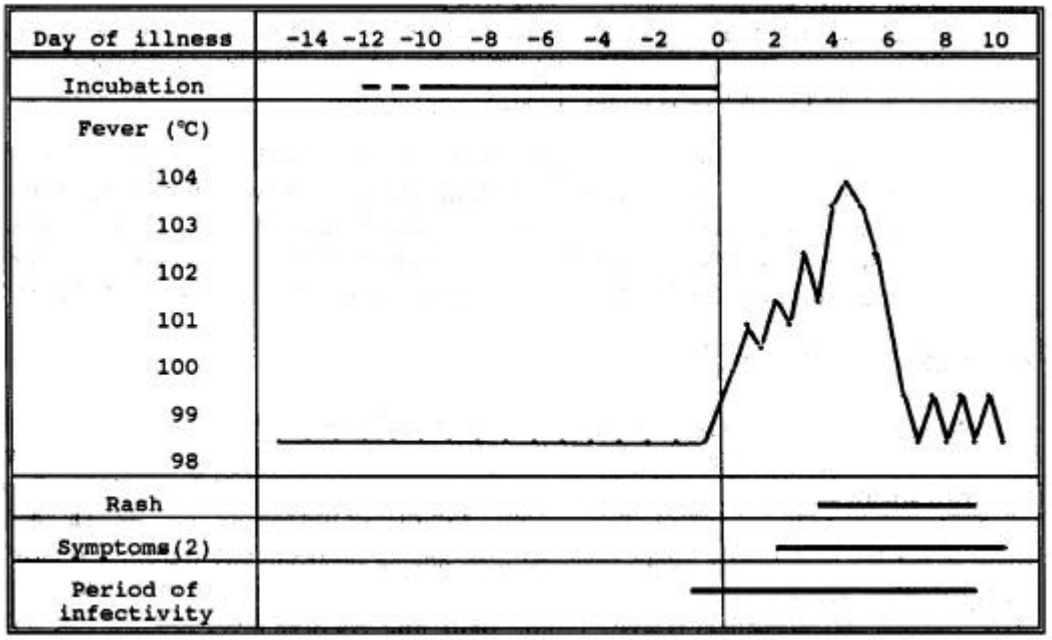
As noted previously, the virus is secreted in the nasopharynx and released in aerosolized droplets upon coughing. Several studies have demonstrated that infection can occur by airborne spread without face-to-face contact with a case. Indeed, measles transmission has been documented in situations where a measles case patient left the room up to two hours prior to the arrival of persons who subsequently acquired infection (Bloch, 1981; CDC, 1983a, 1983b, 1984, 1987; Chen, 1989, Remington, 1985; Sienko, 1987). In a US high school, a child with a vigorous cough caused an explosive single-generation measles epidemic among 69 non-immune children, many of whom had no direct contact with the index case but shared the same corridors between classes (Chen, 1989).

Because measles patients are contagious from three to five days before rash onset (one to two days before the onset of fever and other symptoms), it is often difficult to identify infectious patients, many of whom may still exhibit non-specific symptoms (Figure 1).

3.2 Age and severity of disease

Measles transmission is facilitated by human proximity or crowding (Greenwood, 1988), as may occur in busy clinics. The increased risk of severity of measles disease in crowded conditions has been well-documented in developing countries (Sharma, 1984; Aaby, 1984, 1986, 1988; Lamb, 1988; Garenne, 1990). Indeed, crowding (a proxy for the intensity of the dose of virus received) appears to be more important than nutritional status (a proxy for host resistance) in determining the severity (Aaby, 1986; Lamb, 1988). Other studies have shown that complication rates from measles as well as case fatality rates were significantly higher, and recovery times longer, in infants and young children who acquired measles nosocomially compared to those who acquired disease in the community (Glyn-Jones, 1972; Foulon, 1986; Reynolds, 1987; Hussey, 1990).

Figure 1. Clinical course of measles (1)



(1) Adapted from Krugman and Ward, 1973, and Benenson, 1990. Day 0 corresponds to the end of the incubation period and the start of a rapid replication of the virus as expressed in a rise in temperature and the start of the period of infectivity. Rash and other symptoms follow some days later.

(2) Symptoms: cough and/or coryza and/or conjunctivitis.

In the US during 1983B84, 20% of all measles cases occurred in infants and children too young to have been eligible for vaccination, whereas 59% of all nosocomially-acquired cases during the same period were ineligible (Davis, 1986). Infants and young children may be at greater risk of acquiring measles in medical settings because of more frequent visits to medical facilities, for example, for well-baby clinics. This finding has important implications for the design of recommendations for the prevention of measles transmission in health care settings.

3.3 Characteristics of health facilities

Health facilities play an important role in the transmission of measles, not only within their walls but to the whole community, both in industrialized countries (Bloch, 1981; CDC, 1981, 1983b, 1984, 1986, 1987, 1988; Davis, 1986; Farizo, 1991; Foulon, 1986; Gindler, 1992; Istre, 1987; McGrath, 1992; Mason, 1993; Remington, 1985; Reynolds, 1987; Sienko, 1987) and developing countries (Aaby, 1985; Chen, 1990; Cotton, 1989; Foulon, 1983; Gao, 1988; Guyer, 1976; Klein-Zabban, 1987; PAHO, 1984; Rabelo, 1982).

A five-year retrospective study in the US in the early 1980s found that the greatest proportion of nosocomially-acquired measles infections were reported from hospitals (47%), from physicians' offices (35%) and from out-patient clinics (15%) (Davis, 1986). During community-wide measles outbreaks in two US cities, visiting a hospital emergency room

10–18 days prior to rash onset was a significant risk factor for acquiring disease (Farizo, 1991). Measles transmission also occurred in pharmacies, non-hospital emergency centres, in a drug rehabilitation centre and a laboratory. Forty-five per cent of measles cases evaluated in another US study resulted either directly or indirectly from specific exposure in medical waiting rooms (Istre, 1987). In developing countries, maternal-child clinics have been implicated in the nosocomial spread of measles (Foulon, 1983; Guyer, 1976).

The documentation of measles transmission by airborne spread underscores the importance of the physical organization of medical settings to prevent non-immune children from coming into contact with children who are incubating measles disease. Studies of measles outbreaks in the US revealed that low relative humidity and the lack of fresh air circulation in the waiting room appeared to facilitate measles transmission (Remington, 1985).

3.4 Role of health staff

While most nosocomially-spread measles outbreaks involve non-immune health facility attendees, non-immune health care providers are often affected, especially in countries where measles has not been endemic for many years (Enguidanos, 1992; Gurevich, 1992; Navarrete-Navarro, 1990; Rivera, 1991; Schwarcz, 1992; Subbarao, 1991). A five-year study in the US in the early 1980s revealed that, among nosocomially transmitted measles cases, 50% occurred between patients, 37% patient-to-staff, 8% patient-to-visitor, 3% staff-to-staff, and 2% staff-to-patient (Davis, 1986). Staff who acquired measles most frequently were those who had contact with patients or laboratory specimens, including nurses, physicians, laboratory technicians and clerk-receptionists.

In contrast to industrialized countries, many health care providers in developing countries grew up before the era of measles vaccination and are therefore most likely to be naturally immune and unable to contribute to measles transmission in their workplace.

3.5 Prevention through vaccination

If all infants and children were immune to measles upon entering the medical setting, that is, before exposure to a case, nosocomial transmission could not occur. However, using routine vaccination schedules which limit measles vaccination to children nine months of age and older will fail to protect susceptible infants under nine months of age and vaccine failures which occur in the population. In addition, the ascertainment of measles vaccination status among infants and children, especially in developing countries, is complicated by generally low vaccination card-retention rates. The prevention of nosocomially-acquired measles through pre-exposure vaccination therefore requires modifications to the routine vaccination schedule.

Several studies have demonstrated that measles vaccine is effective in preventing the development of clinical measles in exposed individuals if vaccination is carried out within 72 hours of exposure (WHO, 1993b). The rate of protection varied between 68% and 100%. Four studies of household or institutional (including nosocomial) exposure reported protection of 94% or greater. However, the effectiveness of post-exposure prophylaxis among children under one year of age, particularly those less than nine months of age, has not been studied. Nevertheless, these findings support recommendations to vaccinate exposed individuals with measles vaccine within 72 hours of exposure (American Academy of Pediatrics, 1991).

4. Recommended strategies to minimize nosocomial transmission

While the public health importance of nosocomial measles transmission has been established in many situations, it is clear that, due to a number of limiting factors described above, including the highly contagious nature of the disease in the pre-prodromal phase, it will *not* be possible to eliminate nosocomial transmission entirely. However, a number of strategies are available to minimize nosocomial spread.

Fundamentally, it is vital to maximize awareness among health facility staff that a measles case could enter the facility at any time and to assume that a constant risk of nosocomial spread of measles to non-immune persons exists. In response, health facility staff should maintain a constant state of preparedness to minimize the risk of nosocomial infection.

The following recommendations are divided into two groups: recommendations which are generally applicable, and some additional recommendations which may be suitable only for industrialized countries where more resources are available.

4.1 General recommendations

4.1.1 Maintain high measles coverage in the community

The primary mechanism by which nosocomial spread of measles may be minimized is to prevent the accumulation of susceptible individuals by maintaining measles vaccination coverage in the community as high as possible. Several operational strategies for achieving high coverage have previously been described in detail (WHO, 1993a). According to the epidemiological conditions prevalent and resources available in a specific country, or province or state within a country, a combination of strategies may be required including routine vaccination, special actions for high-risk groups or areas and national immunization days.

Since there are virtually no contraindications to measles vaccination, measles vaccine should be administered regardless of patients' health status. Vaccination with measles vaccine is particularly important for malnourished children and those with chronic illness, as they are at an increased risk of measles complications.

4.1.2 Reduce the age of vaccination during outbreaks

WHO recommends that the age of administration of measles vaccine be lowered to six months while measles outbreaks are in progress in the community. Vaccine should be administered any time after completing six months of age and, for infants vaccinated between six and nine months of age, a second dose should be administered as soon as possible after

completing nine months of age (in industrialized countries, at 12 or 15 months of age, depending on national schedules), provided that at least four weeks have elapsed since the last dose. The second dose at nine months of age is important because the serological response to a dose given before the recommended age of immunization may be significantly lower, resulting in lower levels of protection. Parents should receive instructions to this effect at the time the early dose is administered. *[This procedure concerning revaccination of children vaccinated before nine months of age also applies to sections 4.1.3 and 4.1.4 below].*

4.1.3 Eliminate missed opportunities for vaccination

Missed opportunities for vaccination should be completely eliminated by routinely checking the vaccination status of all children attending any health facility for any reason. This recommendation should be implemented at all immunization clinics, physicians' offices and public and private clinics, health centres and hospital emergency and outpatient wards.

A history of measles disease is not a sufficient reason to defer vaccination since physicians, health care workers, mothers and other caretakers occasionally mistake other fever and rash illnesses for measles. Furthermore, a verbal history of measles vaccination is not reliable and is insufficient to contraindicate vaccination B only card-documentation should be accepted.

In developing countries, where vaccination cards or clinic records are often missing, local conditions should be evaluated when determining the criteria for administering measles vaccine to children whose vaccination status cannot be verified. In general, it is recommended that during a measles outbreak all children aged six months to nine years without documented evidence of measles vaccination receive measles vaccine (see section 4.1.2). In the absence of measles outbreaks, it is recommended that all children aged nine months to *at least* two years without documented evidence of measles vaccination receive measles vaccine.

Ten major causes for missed opportunities for vaccination have been identified (Hirshorn, 1990):

- health workers' use of false contraindications;
- health workers' incorrect screening of vaccination cards;
- vaccine unavailable at the clinic;
- clinic too crowded, disorganized or understaffed;
- cancellation of a scheduled immunization session;
- mothers too busy to wait, misinformed or alienated;
- health workers' refusal to open a vial for few children;
- health workers' acceptance of a verbal history of measles;
- health workers' failure to administer antigens simultaneously;

- failure to vaccinate a child identified as eligible to receive vaccine because the completed vaccination card was returned before vaccine was administered and the parent/guardian misunderstood that the child should wait.

A simple methodology is available for assessing the extent of missed opportunities for vaccination (WHO, 1986b). Systematic efforts must be made to eliminate all missed opportunities for vaccination. Any child eligible for measles vaccine (or other antigens, or any woman eligible for tetanus toxoid) must receive the appropriate catch-up dose(s) before leaving the facility. Even if a non-immune person is inadvertently exposed to measles through direct or indirect contact with a case, measles vaccine will provide protection if administered within 72 hours of exposure.

4.1.4 Ensure adequate measles vaccination status among hospitalized patients

The vaccination status of all hospitalized patients should be rigorously checked. WHO recommends that, in developing countries, a dose of measles vaccine be given to *unvaccinated* infants aged six months to nine years upon admission to hospital, even if there is documented evidence of previous measles vaccination, but the precise age range may be adjusted in light of local conditions (see section 4.1.2). In industrialized countries, only those admitted patients who lack documentation of vaccination need be vaccinated.

Even under ideal circumstances, measles vaccine is associated with an efficacy of 80B90% in developing countries (Hull, 1983; PAHO, 1984; WHO, 1984; Dabis, 1988; Thapa, 1992). Greater levels of protection may therefore be achieved by administering an extra dose of measles vaccine to *vaccinated* infants and children upon admission to hospital, thereby reducing the likelihood of vaccine failure which may lead to nosocomial transmission.

In addition, to guarantee that no opportunities are missed, the vaccination status of patients should be checked again before discharge. Vaccination of those without documentation of previous measles vaccination will reduce the chances of a child returning home while incubating a nosocomially-acquired measles infection. Failure to do this could result in the infection of children in the community with measles originating in the hospital.

Exposed non-immune contacts of hospitalized measles cases, such as patients sharing the same ward and visitors, aged six months to nine years should receive one dose of measles vaccine, where possible, within 72 hours of exposure (see section 4.1.2). WHO does not recommend the use of hyper-immune measles gamma globulin (IMGG), since it is less effective and more costly than measles vaccine for use with non-immunocompromised patients.

4.1.5 Isolate fever and rash cases upon arrival

Cases of fever and rash should be considered as suspected measles until proven otherwise. Differential diagnoses include dengue fever, meningococcal meningitis, rubella, and other viral exanthema. To reduce the chance of exposure, cases of fever and rash presenting at a health facility should preferably not enter the common waiting areas. Where available, such cases should be fitted with a mask and taken directly to a different room reserved for diseases subject to respiratory isolation. Alternatively, where female literacy is more common, a sign may be mounted outside the health facility instructing parents/guardians bringing a child with rash to wait outside and ask another attendee to inform the staff that the child has arrived.

To reduce the severity and risk of complications following measles illness, vitamin A supplements should be administered to all children admitted to hospital who are suspected of having measles (see Annex).

4.1.6 Inform the health authorities

Measles is a reportable disease in almost all countries. All cases of measles should be reported promptly to the district health authorities in accordance with local procedures. In addition, where appropriate, nosocomially-acquired measles cases should be reported immediately to hospital infection control authorities for immediate investigation and response.

4.2 Specific recommendations for industrialized countries

4.2.1 Ensure adequate measles vaccination status among health facility staff

To prevent nosocomial spread of measles in the hospital setting, all staff should be immune. Any staff member who cannot provide documentary proof of measles vaccination or adequate measles antibody titres at the time of employment should receive measles vaccine. There is no increased risk of adverse events associated with administering measles vaccine to individuals who have had measles disease or who have been previously vaccinated.

4.2.2 Separate sick and well children attending health facilities

Where resources permit, sick and well children attending health facilities should be physically separated in different waiting areas to reduce the chance of nosocomial measles transmission. However, care should be taken to ensure that these two groups do not subsequently share the same room or same staff for weighing, clinical examination, vaccination or other consultation, since this would clearly defeat the purpose of their initial separation by allowing the possibility of airborne measles transmission.

4.2.3 Administer gamma globulin to immunocompromised contacts of measles cases

Due to the risk of overwhelming viraemia, live virus vaccines such as measles vaccine are contraindicated in individuals with congenital disorders of immune function or those receiving immunosuppressive therapy. Hence, immunocompromised contacts of measles cases should receive hyper-immune measles gamma globulin (IMGG), as soon as possible after exposure. However, persons infected with the human immunodeficiency virus (HIV) or with suspected or confirmed acquired immunodeficiency syndrome (AIDS) may receive live measles vaccine without risk.

4.2.4 Improve ventilation in health facilities

Ideally, a quarantine area with a separate entrance, waiting, examining and treatment areas and toilets should be included in the design of health facilities to prevent nosocomial spread of infectious diseases such as measles. Where only a common waiting and examining area is available in a health facility, a number of air-flow engineering modifications have been proposed in order to clear the air of aerosolized measles virus and hence reduce the risk of disease transmission. However, such high-cost and/or high technology solutions are dependent upon the availability of resources and are therefore suggested by WHO but not recommended at this time.

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Annex:
Vitamin A therapy

Vitamin A therapy has been shown to reduce significantly the risk of complications (Hussey, 1990) and death (Fawzi, 1993) during measles disease. Clinical trials published to date have shown that vitamin A therapy resulted in a 65% reduction in the measles case fatality rate.

Immediately upon diagnosis, children with measles should receive vitamin A in the following situations:

- in areas where the case-fatality is greater than 1%;
- in areas of known vitamin A deficiency; or
- in any case of severe or complicated measles.

Vitamin A supplements should be administered to all children admitted to hospital with measles: by definition, they are already thought to be ill enough to need further care, and experience shows they are more likely to develop severe complications and die.

Vitamin A supplements are available either as capsules (50 000, 100 000 or 200 000 IU per capsule) or in liquid form with a pump dispenser. Capsules need to be opened for children under the age of two years. Capsules have the advantage that they can be given to mothers for use at home.

The WHO/UNICEF guidelines for dosage are presented in Table 2.

Table 2. Vitamin A therapy for measles cases

Age	Immediately on diagnosis	Next day
Infants <6 months	50 000 IU	50 000 IU
Infants 6B11 months	100 000 IU	100 000 IU
Children ≥12 months	200 000 IU	200 000 IU

- Give the first dose of vitamin A directly to the child. The reason for the second dose is to make sure that the body stores are built up again, even if the child has diarrhoea and is very ill.

- For children not admitted to hospital, instruct the mother about the administration and importance of vitamin A, as the second dose may have to be given at home. Avoid a second visit to the clinic in order to reduce the risk of nosocomial spread of measles to other children.

- High-dose vitamin A supplements are contraindicated for pregnant women.