

# National plan of action to prevent the spread of measles and rubella

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# Foreword

The National Board of Health and Welfare has been commissioned by the Government (S2012/6492/FS, S2013/2531/SAM) to draw up and coordinate a national plan of action that aims to prevent the spread of measles and rubella in the country pursuant to the undertaking made within framework of the World Health Organisation's (WHO) efforts to eliminate these diseases. The assignment has been carried out in collaboration with the Swedish Institute for Communicable Disease Control (The Public Health Agency of Sweden from 1st January 2014), the Swedish Association of Local Authorities and Regions, County Medical Officers and other parties. The assignment shall finally be presented to the Government Offices (Ministry of Health) by 30th April 2014.

A working group of relevant agencies, stakeholders and vaccine experts have produced a broad survey during the year, which forms the basis of this plan of action. The survey has identified important issues and will also be the starting point for a future documented knowledge base to support the health and social care authorities.

The purpose of this plan of action is to clarify:

- objectives and strategy for the Swedish communicable disease work in terms of measles and rubella
- which stakeholders in the field of communicable disease are responsible for individual parts of the overall work
- measures within strategically important areas.

This plan of action initiates the process to complete Sweden's commitment to contribute to WHO's objective to eliminate measles and rubella.

The follow-up shall, according to WHO, take place through a national verification committee responsible for an annual report regarding the diseases, immunisation coverage and immunity. Sweden, Norway and Denmark plan to form a joint verification committee, which in future will audit all three countries' annual reports and plans of action. Implementation will be performed within normal operations.

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## Summary

Measles and rubella are viral infections that only can affect humans. There is no specific treatment, but there are effective vaccines. The World Health Organisation (WHO) considers that there are prerequisites for elimination of the diseases through immunisation programmes, which is now part of the organisation's long term objective.

Sweden has not had a continuous domestic spread of measles or rubella since the end of the 1980s. Immunisation coverage is high and on the basis of national cross-sectional surveys immunity has been assessed to be generally good. At the same time, import-related cases of disease have led to several major outbreaks of measles in recent years. The number of cases in different age groups shows that the two diseases no longer should be considered as children's diseases, even though the majority of those who become ill are unvaccinated children. With a spread of infection among adults there is an increased risk of healthcare-associated infections. A growing risk group, which is dependent on herd immunity against measles, are persons with reduced immunity to infections, particularly patients treated with immunosuppressive drugs. A cessation of the circulation of rubella in Sweden provides protection to unvaccinated women in the country, however not if they travel to countries where the disease is circulating. In 2011, the first case in three decades was reported, where a child was born with severe injuries of rubella, after an unvaccinated woman was infected during an overseas trip during early pregnancy.

The establishment and maintenance of a high level of public confidence in the immunisation programme in general and vaccination against measles and rubella in particular is a prerequisite to reduce the spread of infection and to contribute nationally to the implementation of WHO's global objective for elimination, and it will also be one of the greatest challenges. Accordingly, an important intermediate target in the elimination of measles and rubella is to reach and maintain very high coverage (more than 95 per cent) with two doses of measles vaccine and at least one dose of vaccine against rubella. This demands improved availability and use of evidence-based information to the profession and to the general public, about the advantages and risks associated with vaccination against measles and rubella. Targeted efforts are needed to identify groups with low immunisation coverage and to put tailored measures in place, for example, targeted communication initiatives. Such initiatives are, for example, the promotion of initiatives on local and individual levels in areas with consistently low immunisation coverage through, among others, strengthening resources at vaccinating units (Child Health Centres).

Another important intermediate target is to offer vaccine against measles and rubella, including supplemental vaccination to all sections of the populations at risk of and susceptibility to measles and rubella. This applies to

groups with increased risk of being exposed, such as people travelling abroad, and health care professionals as well as persons who for different reasons may have a lower degree of coverage, for example, community fostered children and newly arrived refugees. Children under 18 months who have not yet received their first vaccine dose are a special problem. The higher number pregnant women who have vaccine induced immunity, the earlier the infant's antibodies from the mother subside. This requires a documented knowledge base and a standpoint on the optimal timing for the first dose.

Strengthening monitoring systems through strict case studies and laboratory verification of suspected individual cases and outbreaks is becoming more important when approaching the elimination of measles and rubella. A basic problem is that increasingly rare diseases disappear from the clinical awareness of health care professionals, which creates an increased need for knowledge support for both health care and virological laboratories.

Bolstering procedures for outbreak management and contact tracing will also increase in importance in a phase, when individual cases are becoming rare. Clear plans are needed to manage both outbreaks and contract tracing of individual cases, including guidelines for the use of immunoglobulin as post-exposure prophylaxis.

## Measures to prevent the spread of measles and rubella within the country

- Provide information to support individuals in making informed decisions and thereby hopefully retain a high level of acceptance and adoption of the MMR vaccination within the framework of the national immunisation programme.
- Draw-up information activities targeted at groups with low immunisation coverage.
- Draw up a plan of action for situations with low immunisation coverage among children.
- Draw up guidelines aimed towards offering supplementary vaccination to adults who have not been vaccinated with two doses.
- Implement targeted sero-immunity studies (adults and children) in areas or groups with low immunisation coverage.
- Produce training materials for health care and vaccination centres on the importance of MMR being included in the basic cover when travelling abroad.
- Develop a documented knowledge base for the timing of the first dose of MMR vaccine.
- Evaluate the timing of the national programme for the first dose of the MMR vaccine to children.
- Act for a wider implementation of health screening of new arrivals including a check if there is a need for MMR vaccination.
- Act for a faster implementation of health screening of newly arrived children.

- Develop guidelines that support employers and health care providers on staff vaccination based on risk analysis.
- Joint follow-up by the Swedish Work Environment Authority and the Health and Social Care Inspectorate of the work environment and health care hygiene procedures. Review the risk group strategies for immunocompromised persons and women who after examination are found to lack immunity to rubella.
- Investigate the possibilities to include testing for rubella in the National Board of Health and Welfare regulations on infection-screening of pregnant women (SOSFS 2004:13).
- Implement systematic follow-up of measles cases with the aim to increase our knowledge on long-term vaccine induced immunity.
- Develop knowledge support for health care and virological laboratories about diagnosis in acute rash illness with fever, and reporting and laboratory verification.
- Annual summary of results relating to immunity to rubella during pregnancy from all laboratories as part of the national vaccine follow-up.
- Act for comprehensive documentation of vaccine that has been given both within and outside the framework of the national immunisation programme.
- Investigate the possibilities of how MMR vaccinations that have been given in another country can be documented and monitored in Sweden.
- Act for a review, on EU level, of guidelines for post-exposure prophylaxis with immune globulin against measles. In collaboration with the Swedish Society for Communicable Disease Prevention and Control, draw up a plan of action for contact tracing and outbreak management of measles and rubella.
- Assist in outbreak management during significant epidemics across country borders.
- Develop consensus documents within the national communicable disease control for the management of outbreaks of measles on aircraft.
- Conduct modelling studies to assess the risk for measles outbreaks.
- Follow-up of epidemic contingency planning and outbreak management.

# Need for a national plan of action to prevent the spread of measles and rubella

## Small but increasing disease burden

Globally, measles is a major cause of death in young children. The World Health Organisation (WHO) reports that 122,000 children worldwide died from measles or complications of the disease in 2012. That represents 330 deaths each day from this infection – 14 deaths every hour around the clock. More than 95 per cent of these deaths occur in low-income countries often with inadequate health structures [1].

In Europe, nearly all cases of measles in recent years have occurred in Bulgaria, France, Ukraine, Romania, Italy, UK, Spain, Germany, Russia and Switzerland. In 2012, nearly 24,000 cases of measles were reported to WHO's European Region [2]. The number of children born in Europe with injuries caused by the rubella virus is unknown due to varying monitoring and reporting systems, however, in the world WHO estimates that each year a total of some 110,000 children are born with so called congenital rubella syndrome (CRS) [3].

In Sweden, both diseases declined quickly when general immunisation of children with two doses of combined vaccine against measles, mumps and rubella was introduced in 1982 and since the late 1980s, we have not had any continuous domestic spread of the infection [4]. However, every year we see cases where people have been infected abroad. Usually 0–5 cases per year of rubella, and some additional cases of measles. Occasionally, imported infections cause secondary cases in one or more stages. In recent years, this has resulted in several outbreaks of measles, most of which also spread in health care, and one major outbreak of rubella. During 2012, in total 50 cases of rubella and 30 cases of measles were reported in Sweden, which was then the highest number of cases since 2000. 2013 was another record year for measles, with 51 cases reported. During the last 15 years, a total of more than 300 measles cases have been reported, of which about half among unvaccinated children. A child with severe rubella-induced fetal damage was born in 2011 [5].

## Measles – severe general infection with the risk of complications

For individuals with immunosuppressive treatment measles can be life threatening. Even in a healthy immune individual measles frequently gives a severe general infection. The risk of the most serious complications such as encephalitis or death is stated to be one or two per thousand. Common complications are diarrhoea and pneumonia, which can be caused by bacterial

infections and/or the virus itself. The measles virus can cause a persistent increased risk of other infections for several months after measles. There is also a late form of brain inflammation that develops first several years after a seemingly uncomplicated measles infection and which is always fatal, this is also known as SSPE (subacute sclerosing panencephalitis), where the risk is 0.1–1 per 100,000 [6].

### Rubella – mild infection with the risk of fetal damage

The disease is usually a modest viral infection. Older children and adults can have joint pain or arthritis. There are also reports that adults can have a clinical picture that is more reminiscent of measles. Complications such as encephalitis or bleeding in different organs do occur, but are rare (one case per 10,000 patients). If a pregnant woman is infected in early pregnancy there is a risk of more or less severe damage to the brain, heart, eyes and hearing of the fetus. The need of care and rehabilitation efforts in congenital rubella, CRS, can be extensive. The long-term follow-up of children who have been exposed to infection early in fetal life also shows other aftereffects and symptoms such as deafness, autism and other behavioural disorders, metabolic disorders, and 100–200 times increased risk of diabetes [6].

## WHO's elimination goal

Measles and rubella are viral infections that only can affect humans. Thus there are prerequisites to eliminate the diseases through immunisation programmes, which are now part of the WHO's long term goal. WHO's Region of the Americas announced its latest case of indigenous measles in 2002, which proves that elimination could be a possibility also for the European region. WHO's definition of the elimination of the diseases from one country is the absence of continuous circulation for at least one year, and less than one case of illness per million inhabitants per year for three years. Import-related cases are not included.

Within the European region, the goal is to eliminate measles and rubella by 2015 [7], and globally to eliminate both diseases from at least five of WHO's six regions in the world by 2020. [8]

WHO's comprehensive strategy is based on five main components [8]:

1. Achieve and maintain high levels of population immunity by providing high vaccination coverage with two doses of measles- and rubella-containing vaccines.
2. Monitor disease using effective surveillance and evaluate programmatic efforts to ensure progress.
3. Develop and maintain outbreak preparedness, respond rapidly to outbreaks and manage cases.
4. Communicate and engage to build public confidence and demand for immunization.
5. Perform the research and development needed to support cost-effective operations and improve vaccination and diagnostic tools.

## National strategy

In 1982 Sweden and Finland were the first countries in the world to introduce two doses of MMR vaccine in the national childhood immunisation programme. At the same time a recommendation of immunity examination against rubella in pregnant women was introduced, followed by an offer of immunisation to susceptible women after childbirth. The aim of this was to achieve direct protection in pregnant women, because infection with this virus in early pregnancy can cause severe fetal damage. The National Board of Health and Welfare's general advice (SOSFS 1982:13) concerning the diagnostics of and preventive measures against rubella infection summarises the previous Swedish strategy against rubella:

- general immunisation of children with two doses
- testing regarding rubella antibodies during pregnancy
- targeted immunisation of newly delivered non-immune women
- targeted immunisation of non-immune women of childbearing age, if in their professional work, they risk contact with the rubella infection
- diagnosis and measures in the event of suspected infection with rubella virus in a pregnant woman or in her immediate circle.

Even today the basis of the Swedish strategy is the implementation of the national immunisation programme with high immunisation coverage for both doses of the MMR vaccine, and that women of childbearing age are protected against rubella.

The timing of the two doses was revised in 2007, and at the same time the measure was introduced that all children up to 18 years old shall be offered additional vaccination if they have not previously been vaccinated, according to the National Board of Health and Welfare's regulations (SOSFS 2006:22) concerning the immunisation of children. Risk of infection at the workplace follows the regulations of the Swedish Work Environment Authority's (AFS 2005:1) concerning microbiological work environment risks – infection, toxin effects, hypersensitivity. Communicable disease measures are regulated in the Communicable Diseases Act (2004:168) and the Communicable Disease Ordinance (2004:255). The remaining two measures, pregnancy screening for rubella and immunisation of non-immune after childbirth, still follow the National Board of Health and Welfare's general advice from 1982 (SOSFS 1982:13).

Additional parts in the overall strategy have been added. One is the now regulated health examination of asylum seekers and other immigrants. Another is an emerging practice of considering two doses of MMR as part of the basic protection that everyone should have before travelling abroad.

## Primary and secondary prevention

The comprehensive national strategy, which today aims to prevent the spread of measles and rubella within the country, consists both of primary and secondary prevention. The diseases are prevented primarily through vaccination. This applies irrespective of whether the vaccine is given within the

framework of the national immunisation programme, to a woman who has recently delivered and who during pregnancy lacked sufficient rubella antibodies, as a work environment measure or if the vaccine is given prior to travelling abroad. Immunoglobulin administered to measles exposed non-immune persons can in most cases prevent an onset. Rapid infectious disease control measures with advice to individual patients, contact tracing and outbreak management constitute secondary preventive measures. Even hygiene procedures, e.g. triage and care procedures for airborne infection, aim to prevent an infected person from spreading the infection. Testing of pregnant women with acute rash illness makes another type of damage minimisation possible. A rubella infection that is detected during early pregnancy allows information to be given to the parents, after which abortion may come into question.

## Strategic areas

As stated above, the range of measures span varying areas that require the participation and involvement of numerous different stakeholders and authorities. A national plan of action aims to clarify the objectives and strategies for the Swedish infectious disease control efforts and coordinate the essential measures required in strategically important areas to meet WHO's goal of eliminating measles and rubella.

The following strategically important areas are managed:

1. Immunisation coverage
2. Risk groups
3. Monitoring and follow-up
4. Contact tracing and outbreak management

# Immunisation coverage

## High immunisation coverage among children

Among children born in 2009 and 2010, over 97 per cent were vaccinated against measles, mumps and rubella (MMR) at age 2, which is the highest coverage ever. Among pupils in the 6th year of compulsory school during the academic year 2011/12 at least 95 per cent of students had been vaccinated with two doses of MMR vaccine. Reports from the school health service usually comprise 95–97 per cent of students in the year in question. The percentage of totally unvaccinated pupils at 12 years old is about 1 per cent. [9] Accordingly, immunisation coverage among children is high and at a level that provides herd immunity.

The national average of coverage has for three decades been around 96 per cent of children who last year turned 2 years old, with the exception of a temporary decline to 89–91 per cent in 2002–2003. [9] The temporary decline coincided with a public debate whether the MMR vaccine could cause autism that contributed towards some parents choosing to forgo or postpone this vaccination. The debate, which was based on a scientific article that incorrectly drew conclusions about a possible relationship, had an even greater effect on the desire to vaccinate in some other countries, notably Britain. Establishing a high level of confidence in the national immunisation programme in general and immunisation against measles and rubella in particular, is a prerequisite for elimination and will also be one of the greatest challenges.

## Groups with lower immunisation coverage

Since November 2012, the Public Health Agency of Sweden runs a pilot project in collaboration with WHO and European Centre for Disease Prevention and Control (ECDC) to test a new method, *Tailoring Immunization Programmes* (TIP). The method includes specific tools to identify and prioritise non-immune groups, plot factors that hinder and promote immunisation in these groups and to formulate evidence-based interventions from the results. The project mainly includes qualitative studies such as structured in-depth interviews and focus groups, but also studies of media and information search patterns in the population that can form the basis of tailored information initiatives.

The results up until November 2013 indicate different patterns in the municipality Järna and in the Stockholm suburbs of Rinkeby and Tensta, which have been chosen as examples of geographical areas with low immunisation coverage, and illustrate the need of other, more innovative methods, that convey knowledge through existing networks in the local community. Health

care professionals also need relevant methods tailored to target groups to disseminate knowledge of the benefits of vaccination. In addition, in-depth - interviews were held among undocumented immigrants who show a consistent picture of wanting to vaccinate their children, but where there is a fear of being expelled and structural barriers to access health care and thus vaccination (Ann Lindstrand, Public Health Agency of Sweden, personal contact).

## Lower immunisation coverage among community fostered children in Malmö

A health survey of community fostered children in Malmö showed that around 15 per cent of the children in this study lacked one or more vaccinations when they reach school age, including MMR. This represents significantly lower immunisation coverage than average. The percentage of children who had not undergone regular health checks at the school health service was significantly higher for children in care homes or accommodation compared to others [10].

## Incompletely vaccinated

Children up to age 18 shall, with a few specified exceptions, be offered vaccination if they have not previously been vaccinated in accordance with the immunisation programme in the Public Health Agency of Sweden's regulations (SOSFS 2006:22) on vaccination of children. This also applies to measles and rubella, as well as children who have previously been vaccinated against one of the two diseases. The child should then be offered a combined vaccine against measles, mumps and rubella (i.e., MMR vaccine, as separate monovalent vaccines are currently not available).

The school health service is responsible for the period when the child goes to school and the county council is responsible for children that are not covered by the school health service. Supplementary vaccinations are to be offered free of charge and vaccinations given from 2013 are reported to the immunisation register for each child.

Currently, from the age of 18 there is no general right to free supplementary vaccination. However, the Work Environment Act prescribes that an employer is responsible for making a risk assessment of microbiological risks such as infectious diseases at the workplace, and to offer free of charge preventive measures and health checks as warranted by the risk assessment. According to AFS 2005:1 this applies to both health care professionals and students enrolled in nursing education. It is not mandatory for county councils to provide adult females of childbearing age with supplementary MMR vaccination if they have no protection against rubella. Some county councils do offer this free of charge.

## Measures

- Provide information to support individuals in making informed decisions and thereby hopefully retain a high level of acceptance and adoption of the MMR vaccination within the framework of the national immunisation programme. (*National Board of Health and Welfare, Public Health Agency of Sweden and the Medical Products Agency*).
- Draw-up information activities targeted at groups with low immunisation coverage (*Public Health Agency of Sweden*).
- Draw up a plan of action for low immunisation coverage among children (*Public Health Agency of Sweden*).
- Effect better coordination between social services and health services for children in community care, and information initiatives directed towards health care providers on all levels, so that the patient is always asked about their current vaccination status, especially those with a background from another country, new arrivals and people staying in the country without a permit (*Health and social care authorities*).
- Draw up guidelines aimed towards offering supplementary vaccination to adults who have not been vaccinated with two doses (*National Board of Health and Welfare*).
- Implement targeted sero-immunity studies (adults and children) in areas or groups with low immunisation coverage (*Public Health Agency of Sweden*).
- Produce training material to health care and vaccination centres about the importance of MMR being included in the basic cover when travelling abroad (*National Board of Health and Welfare and the Public Health Agency of Sweden*).

## Risk groups

There are two types of risk groups. One concerns who is at risk of being infected by a disease and the other concerns who is at risk of then becoming extremely ill.

### Increased exposure to infection

#### Infection abroad

Out of 179 cases of measles reported to the then Swedish Institute for Communicable Disease Control during 2004–2013 infection in Sweden, was declared in 99 cases and infection abroad in 74 cases; there is no data for the remaining six cases. For those who were infected abroad, 30 different countries were stated as the source country of which the most common were: Thailand (15 cases), France (8 cases) and the UK (5 cases) [5].

#### Infection within health care

Health care personnel are, on account of their work, at an increased risk of exposure to measles and rubella. According to a recently published international survey, it was estimated that the risk of being infected with measles was 2 to 19 times higher for non-immune health care personnel compared with the general population. During the period 1989–2014, 53 articles have been published where the spread of measles has been identified from patients to health care personnel, while 18 articles gave examples of disease transmission from health care personnel to patients or to other health care personnel [11]. In Sweden, according to the Public Health Agency of Sweden, six health care workers fell ill with measles during 2012–2013. Different professional groups were represented among those who had fallen ill, not just those with direct patient contact. Everyone became infected at their workplace within the country (Tiia Lepp, Public Health Agency of Sweden, personal contact).

Patients with fever, respiratory symptoms or rash must be taken directly to a separate room for examination and treatment at all clinics for children and adults, within primary care, hospital care and other forms of care, such as local medical and dental centres. This applies to both emergency and planned visits. It is the duty of the health care provider to ensure that facilities and the organisation conform to this requirement. Within inpatient care in each county council there must be a sufficient number of single rooms with special ventilation to be able to care for patients with confirmed and suspected measles (the number of rooms must also meet the need for the care of patients with tuberculosis and other airborne infections). These requirements are evident from the Health and Medical Services Act (1982:763), Dental Care Act (1985:125) and Patient Safety Act (2010:659).

## Insufficient immunity

### Children and adults are affected by measles

During 2007–2012 the age distribution among the 91 measles cases ranged from 8 months to 58 years. Most cases were reported in the age group 0–4 years, of which eight were under the age of 1 year old and thus too young to be vaccinated against measles; ten were over 18 months and therefore had been vaccinated in the national immunisation programme and nine were 12–18 months. An additional 18 children had not been vaccinated, despite being between 19 months and 19 years old, i.e. at an age when most should have been offered additional vaccination (up to 18). Nearly half, 42 cases, were over 20 years old. In an analysis of the year of birth in measles cases during 2000–2012, the number of cases among unvaccinated age groups was largest among those born in the 60's, i.e. individuals who were children when the measles virus was no longer circulating to such a large extent [5].

### Immunity studies

Normally the immunity status is reflected by the disease occurrence, but when a disease is no longer circulating in a country immunity studies are used to assess whether the population has sufficient immunity to resist future exposure or outbreaks due to imported cases of the disease. Antibody concentrations in individuals are then checked in a statistical sample of the population without regard to whether the individuals have been vaccinated or not, to evaluate immunity in different age groups or in specific risk populations.

The last two cross-sectional studies were conducted in 1997 and 2007 [12, 13]. According to the survey in 2007, more than 98 per cent of the participants had measles antibodies above the protective level, while 95 per cent had a protective level of antibodies against rubella. Both studies identified higher average antibody concentrations in age groups that typically have had measles or rubella, compared to those who had received their immunity primarily through vaccination.

The study also shows that the concentrations of measles antibodies decline from 6–7 years of age and that a high percentage of children aged 8–11 years are below the immunity threshold. This fact supports the decision that from 2007 the booster dose be moved forward from being given at 12 years old to now being given at 6–8 years of age. However, there are fears of an increased risk for women being susceptible during pregnancy as a result of the second dose of MMR being moved forward. Therefore it is especially important to follow the immunity status.

The studies in 1997 and 2007 also included umbilical cord blood, which shows the degree of antibodies transferred from mother to child. In 2007, rubella antibodies were identified to be above the immunity level in a total of 96.5 per cent of umbilical cord samples taken from women aged 18–40 years.

**Table 1. Probable immunity to measles or rubella among persons born in Sweden during different periods and grown up in the country**

Before 1960	1960s	Year of birth 1970–1980	1981–2001	From 2002
Most people are immune to measles once the infection has run its course, many are immune to rubella.	Varying immunity, many may be non-immune Girls born from 1963 have usually received one dose of vaccine against rubella at school (started in 1974.)	Most children have received 1 dose of MMR at school at the age of 12.  Some have even received 1 dose of measles vaccine during infancy (started in the 1970s, but with varying degrees of impact).	Most children have received 2 doses of MMR (introduced in 1982).  Dose 1 given at 18 months, dose 2 at approximately 12 years.	Most children have received 2 doses of MMR.  Dose 1 given at 12-18 months, dose 2 at 6–8 years of age.  From 2006, children up to 18 years are to be offered supplemental doses if not previously vaccinated under the programme i.e. with 2 doses MMR.

Source: National Board of Health and Welfare (Socialstyrelsen)

## Not yet vaccinated infants

Infants have protection against measles through antibodies transferred to the baby during pregnancy a.k.a. maternal antibodies. The more pregnant women who have a vaccine induced immunity, the earlier the infant's antibodies from the mother subside. As a consequence there may be a risk that the child does not have adequate protection during the last months before the current time of the first MMR dose, i.e. at 18 months. In the summer of 2013 the spread of infection among children aged 12–17 months was identified in Malmö.

In Finland the Institute for Health and Welfare (THL) recommends that the first dose be moved forward and given at 12 months of age [14]. Meanwhile, it must be noted that a general advancement may pose a risk of impairment of the long-term protection to those who are vaccinated. During an outbreak in Canada, children who had received two doses were at a greater risk of contracting the disease if the first dose was given at 12–13 months of age rather than at 15 months of age [15].

## Waning immunity after vaccination

Anyone who has had one of the diseases has lifelong immunity against the disease. Immunity after vaccination works in the same way as after illness i.e. induces both specific antibodies and cell-mediated immunity against the measles virus. The difference is that the vaccine virus is attenuated and therefore the immune response is not as strong. Both Swedish and international sero-immunity studies have shown that antibody levels against MMR are

lower after vaccination than after the infection running its course. There are no reliable data to assess the risk of immunity to measles or rubella subsiding completely. When the vaccines were developed and evaluated in efficacy trials, the diseases were still circulating and improved the vaccination protection. In the absence of such natural boosting, antibody concentrations decrease over time after vaccination. If this is of clinical significance, it will be manifested in countries that have been in the elimination phase for the longest period of time, including Sweden.

### Specific groups

A study on women in southern Stockholm shows that 8.2 percent of Swedish women born after the introduction of general immunisation had antibody levels against rubella below the threshold for immunity. The corresponding share for women born outside of the Nordic countries was 7.7 percent and for newly arrived immigrants and asylum seekers 10.2 percent. Among foreign-born established in Swedish society, the percentage with antibodies below the immunity limit is still higher than among Swedish-born, but slightly lower (4.2 percent) than among the new arrivals (7.2 percent) [16].

In a separate sero-epidemiological study from 2007, the Public Health Agency of Sweden studied whether foreign-born children aged 14–16 years had equally good immunity against diseases included in the childhood immunisation programme as Swedish-born children who were [17]. The children in the study had all arrived in Sweden after the age of 6 years. The results suggest that immunity is as good in both groups. In all probability the foreign-born were naturally infected by many of the diseases in their countries of origin. In many cases, the antibody profiles show that the foreign-born have also received a booster dose of vaccine later than children born in Sweden. In other words, the study suggests that they in fact probably have a better immunity than Swedish-born children, but the results should be interpreted with caution, particularly as it had a large shortfall, which could mean that there may be new arrivals who are susceptible to the diseases.

In order to analyse the significance of foreign origin for the reported cases of measles, the National Board of Health and Welfare requested information from Statistics Sweden for the 314 measles cases reported from 1997 to 2012. Of the 280 cases where there was access to the complete personal or coordination number, 232, i.e. 83 per cent were born in Sweden. About two-thirds of the 46 foreign-born came from Europe, 9 from the Nordic Countries and 20 from other parts of Europe. Of 37 adults with a foreign background, defined as two foreign-born parents, 26 had at least a ten-year stay in Sweden.

## Increased risk of serious illness with infection

How measles develops is mainly dependent on the ability of the individual's immune system. Even immune healthy persons can in rare cases suffer complications or even death. The risk of a complicated course of illness is higher in generally sensitive groups, for example, among infants or pregnant wom-

en, and especially in people with a compromised immune system. Above all this applies to individuals with inadequate cellular immune response. At the same time, these are groups that are difficult to protect through direct vaccination and where protection is largely dependent on herd immunity.

## Measures

- Develop a knowledge base for the timing of the first dose of MMR vaccine. (*Public Health Agency of Sweden , Medical Products Agency*).
- Evaluate the timing of the national programme for the first dose of the MMR vaccine to children (*National Board of Health and Welfare*).
- Act for a wider implementation of health screening of new arrivals and then check whether there is a need of MMR vaccination. (*National Board of Health and Welfare*)
- Act for a faster implementation of health screening of newly arrived children (*National Board of Health and Welfare*)
- Develop guidelines that support employers and health care providers on staff vaccination based on risk analysis. (*Swedish Work Environment Authority's website*)
- Joint follow-up by the Swedish Work Environment Authority and the Health and Social Care Inspectorate of work environment and health care hygiene procedures (*Swedish Work Environment Authority and Health and Social Care Inspectorate*).
- Review the risk group strategies for immunocompromised persons and women who after examination are found to lack immunity to rubella (*National Board of Health and Welfare*)
- Investigate the conditions to include testing for rubella in the National Board of Health and Welfare regulations concerning infection screening of pregnant women (SOSFS 2004:13) (*National Board of Health and Welfare*).
- Implement systematic follow-up of measles cases with the aim to increase our knowledge about the long-term vaccine induced immunity (*Public Health Agency of Sweden*).

## Monitoring and follow-up

Having a global elimination goal for the immunisation programme puts new demands on follow-up. However, the follow-up of measles and rubella is performed according to the same basic principles as for all diseases covered by national programmes. The main purpose is to verify that the national immunisation programme meets the objectives and expectations on both the impact of the programme and its implementation. The available tools for collection and analysis used are the same as for other diseases and are based on five pillars: monitoring the incidence rate, immunity, immunisation coverage, vaccine safety and microbiology, of which the first three are most important in this context.

### Incidence rate

Monitoring of cases is based on the reporting of cases, which presupposes that the health services recognise and diagnose patients with measles and rubella. Since the introduction in the national immunisation programme, cases of measles and rubella have become rarities and the diseases are therefore no longer part of the clinical consciousness as before. Maintaining a high level of awareness in the health services is a major challenge and a prerequisite for achieving an elimination goal.

From a follow-up point of view, it is important that each occurrence of the disease is regarded as a case that potentially could have been prevented. This approach allows for an analysis on the same principle as for non-conformity management in health services, i.e. an event analysis. The question is then whether the individual has been reached or not by the offers of vaccination and measures that should have been followed by the different parts of prevention. Outbreak investigations contribute towards important empirical knowledge in terms of infectious diseases' epidemiology and the effects of disease control work. It is important that the experiences from the outbreak management are compiled and preserved. Currently there is no structured system for reporting outbreaks over and above the information recorded on the individual illness case.

The importance of a more thorough follow-up of outbreaks is reflected in the World Health Organisation's (WHO) requirements on member countries. For the chain of infection and outbreaks, WHO asks for an annual review (location, start and end dates, number of people, genotype, and whether the case is import-related or not). A separate outbreak report is required for each major outbreak. WHO's aim is that each suspected or confirmed case of measles or rubella should be managed in the same way as larger outbreaks and investigated immediately with accurate contact and contact tracing, identification of immune status among contacts and any prophylaxis for non-immune individuals to limit the spread of infection [18].

Measles and rubella are diseases that must be reported. A special duty to report for congenital rubella was introduced in 2008 in connection with an amendment of the case definitions for reporting according to the Communicable Diseases Act (2004:168) [19]. Furthermore, the Public Health Agency of Sweden is investigating the possibility of a follow-up programme of CRS through the analysis of antibodies against rubella in children with sensorineural hearing loss, the most common injury associated with CRS.

## Monitoring of immunisation coverage

In an elimination phase with generally high immunisation coverage, the relative significance of vaccines given outside of the ordinary national immunisation programme will increase. The diseases are prevented initially through vaccination against measles, mumps and rubella (MMR). This applies irrespective of whether the vaccine is given within the framework of the national immunisation programme, to a woman who has recently delivered and during pregnancy lacked sufficient antibodies against rubella, as a work environment measure or prior to travelling abroad. The health assessment offered to asylum seekers and others could also help, if those inadequately vaccinated were offered supplementary vaccination.

Since 1981, child health care and school health care follow the adherence to the immunisation programme through a separate annual review of all medical records. Individual registration in the new immunisation registry was started in parallel in 2013 and it will eventually replace the current system for monitoring immunisation coverage. Running the register concurrently with other health data and quality registers will also contribute to the assessment of vaccine efficacy, safety signals, disease burden and health economics.

However, the register will not provide information about the overall immunisation coverage, as it is not possible to register vaccinations that a child has received abroad. MMR vaccinations of adults are not recorded at all. The Public Health Agency of Sweden has requested the Ministry of Health for an extension of the statutory details that may be registered in the immunisation - register (e.g. with dose number and vaccinating health care unit).

## Immunity

Normally, the immunity status is reflected by the disease occurrence, however when the disease is no longer circulating in the country immunity studies become an important tool in assessing whether the population has sufficient immunity to resist outbreaks due to imported cases of the disease. So far, seroepidemiological cross-sectional studies have been conducted at approximately 10-year intervals. Antibody concentrations in individuals have been checked in a statistical sample of the population without regard to whether the individuals have been vaccinated or not, to evaluate immunity in different age groups. The last two cross-sectional studies were conducted in 1997 and 2007 and the next one is planned for 2015 [12, 13]. Seroepidemiological cross-sectional studies are resource intensive and costly; a good reason to

investigate how they can be targeted towards specific subpopulations to answer specific questions, for example, as in the study in 2007 of the immunity status of foreign-born [17]. There is also a need to ensure that the serological diagnosis carried out on clinical grounds are utilised optimally in the follow-up process. The information available regarding sampling for rubella during pregnancy suggests that compliance varied both in different parts of the country and over time.

## Measures

- Develop a documented knowledge base to support the health services and the virological laboratories regarding diagnosis in acute rash illness with fever, and reporting and laboratory verification (*Public Health Agency of Sweden*).
- Annual summary of results relating to immunity to rubella during pregnancy from all laboratories as part of the national vaccine follow-up (*Public Health Agency of Sweden*).
- Act for comprehensive documentation of vaccine that has been given both within and outside the framework of the national immunisation programme (*Public Health Agency of Sweden*).
- Investigate how MMR vaccinations given in another country can be documented and monitored in Sweden (*Public Health Agency of Sweden*).

# Contact tracing and outbreak management

Secondary preventive disease control measures with advice to individual patients, contact tracing and outbreak management make up damage minimisation measures. The objective of outbreak management is, as far as possible, to eliminate the risk of infection in order to reduce morbidity and mortality, provide targeted support to vulnerable groups and individuals and give everyone an opportunity to protect themselves against infection. Hygiene procedures, e.g. triage and care procedures for airborne infection, aim as well to prevent an infected person from spreading the disease. The county councils are the main stakeholders in charge of the management of individual cases as well as outbreak management, and there may be differences within the country in how this secondary prevention is carried out, as in the need for national support and guidance. However, County Medical Officers have expressed a need for guidance documents for the management of cases and outbreaks of measles, particularly the use of secondary prophylaxis.

## Contact tracing

Measles and rubella are diseases that must be reported and contact traced pursuant to the Communicable Diseases Act (2004:168). For measles contact tracing aims to immediately identify non-immune contacts, so they can be offered post-exposure prophylaxis with measles vaccine alternatively with immunoglobulin, and to find those who have fallen ill as early as possible so that they can receive the right care, with the right hygiene procedures. For rubella, the aim above all is to identify possible exposure of early pregnant women for follow-up, as well as to prevent more pregnant women from being exposed. A child with a congenital rubella infection may excrete the virus for 6–12 months and over a longer period if the injury is severe.

There are no specific secondary prophylactic measures for an exposed pregnant woman without immunity to rubella. Post-exposure prophylaxis for exposure to measles with vaccine may come into question up to three days and with immunoglobulin up to six days after exposure. Vaccination against measles and rubella should not be administered to immunocompromised persons, pregnant women and the smallest infants. The effect of the vaccine on infants from 6 to 12 months may be affected by any residual maternal antibodies in the infant. Accordingly, post-exposure prophylaxis with immunoglobulin containing measles antibodies is the only option for these groups and later than 72 hours after exposure. At the onset, despite immunoglobulin prophylaxis, the course of infection usually becomes milder.

There is no longer an immunoglobulin compound that still has the indication post-exposure prophylaxis against measles. Consequently, pharmaceutical producers are not obliged to guarantee a certain level of antibodies

against measles in the product, which in turn means that the effect is uncertain and it is difficult to calculate an appropriate dosage.

## Contract tracing for exposure to measles on aircraft

Contact tracing for exposure to measles during international flights is associated with specific problems. Countries differ in how far they have come in terms of preventing the spread of measles, and there are different views on the impact in relation to the resources required. Experience shows that it is often difficult to acquire the passenger details, that information is often inadequate as a basis to carry out contact tracing and that frequently information is received so late that post-exposure prophylaxis is no longer possible.

## Outbreak management

Outbreaks are sudden and usually unforeseen events, which require a rapid and coordinated secondary preventive intervention to control or stop the infection. Outbreaks of measles may still be difficult to get quickly under control. The initial infection is usually imported from other countries through travellers, who generally are unaware of both a lack of immunity to measles and that they have been exposed to the infection. The high level of infection, in combination with the fact that the disease has become so rare that few recognize it, means that the newly infected may transmit the virus to many others before diagnosis. As the infection is airborne, infectiousness is especially high indoors and thus there is a risk of widespread outbreak if a newly infected person stays in large indoor premises or particularly sensitive environments, such as health care facilities. It can be life-threatening for immunocompromised patients. There is also a work environment risk.

Our three metropolitan regions and Uppsala have all been affected by measles outbreaks in recent years.

In 2008, the most comprehensive contact tracing so far regarding measles was carried out in Gothenburg, after a newly diagnosed schoolgirl spent five hours in a waiting room at the Children's Hospital. In total almost 400 people were contacted, 61 received immunoglobulin and two secondary cases fell ill [20]. Two outbreaks of measles occurred in the Stockholm County Council in 2012 with 16 and five cases respectively. In Malmö five adults and nine children became ill over a two-month period in an outbreak during the summer of 2013. In Uppsala in the spring of 2013, a child became ill who had recently flown to Arlanda airport from the Middle East. It eventually turned out that in all probability the child had been infected by a middle-aged fellow passenger who had, then undiagnosed, measles during the trip home. In Stockholm five cases were discovered and in Uppsala a total of 12 people fell ill, including four adults aged 32–48 years. The outbreak was complicated by the spread of infection within the Uppsala University Hospital and several individuals had been infected during visits to the children's clinic. This led to extensive investigations regarding the status of immunity to measles for personnel within several clinics at the hospital, as well as major vaccination efforts. Despite the fact that even personnel who cared for children with severely reduced infection immunity became ill, of which three received im-

munoglobulin, there was no spread of infection among these patients. None of the patients who fell ill had any serious complications [21].

In 2012 the National Board of Health and Welfare published the report *Beredskapsplanering för utbrott av smittsamma sjukdomar* (Contingency planning for outbreaks of infectious diseases) [22]. The aim was to improve the conditions for cooperation in the event of outbreaks. The form is generic and acts as planning support for how specific plans can be formulated. The focus is on outbreaks on a national level and outbreaks with large regional or local spread as well as outbreaks occurring in the malignant form. A great deal can also be applied to more mundane and local outbreaks. The document contains proposals for development goals, primarily directed towards how collaboration could be improved in order to develop forms of national, regional and local collaboration in outbreaks of communicable diseases. Target groups for this planning support are mainly the communicable disease stakeholders.

## Measures

- In collaboration with the Swedish Society for Communicable Disease Prevention and Control draw up a plan of action for contact tracing and outbreak management of measles and rubella. (*National Board of Health and Welfare and the Public Health Agency of Sweden*).
- Assist in outbreak management during significant epidemics across county borders (*Public Health Agency of Sweden*).
- Develop consensus documents within the national communicable disease control for the management of outbreaks of measles on aircraft (*National Board of Health and Welfare*).
- Conduct modelling studies to assess the risk for measles outbreaks (*Public Health Agency of Sweden*).

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