Measles: A dangerous vaccine-preventable disease returns

ABSTRACT

Although a safe and effective vaccine has been available for over 6 decades, vaccine hesitancy in the United States and social and political unrest globally have led to under-vaccination. As a result, in recent months, vaccine control of measles has been threatened with an alarming upswing in measles cases nationally and internationally. Here, we review the disease and its management in view of recent outbreaks.

KEY POINTS

Measles is highly contagious and can have serious complications, including death.

Measles vaccine is given in a 2-dose series. People who have received only 1 dose should receive either 1 or 2 more doses, depending on the situation, so that they are protected.

The diagnosis of measles is straightforward when classic signs and symptoms are present—fever, cough, conjunctivitis, runny nose, and rash—especially after a known exposure or in the setting of outbreak. On the other hand, in partially vaccinated or immunosuppressed people, the illness presents atypically, and confirmation of diagnosis requires laboratory testing.

Management is mostly supportive. Children—and probably also adults—should receive vitamin A.

Since disease can be severe in the unvaccinated, immune globulin and vaccine are given to the normal host with an exposure and no history of vaccine or immunity.

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alive in the last major outbreak 65 years earlier became ill, but everyone under age 65 was at high risk with “high attack rates,” estimated as 99% from other outbreaks (reviewed by Krugman et al).

In isolated regions previously free of measles, adults did not have immunity, and when exposed, they often developed severe disease. When European settlers brought measles and smallpox to the Americas beginning in the late 15th century, these diseases decimated whole populations of native peoples who had never been exposed to them.

The wide accessibility and promotion of the measles vaccine over the last 6 decades has dramatically decreased the incidence of measles in the United States (Figure 1). The disease was declared eliminated in 2000. That was premature. A number of outbreaks have occurred since then; the largest in the United States (before 2019) was in 2000. Over half of the 667 cases reported during that outbreak were in an underimmunized Amish community in Ohio.

Now it emerges again.

PRESENTATION CAN VARY

Measles is an acute viral illness. In endemic areas or during outbreaks, measles should be suspected in a patient who has the classic triad of the 3 “Cs”: cough, conjunctivitis, and coryza (runny nose).

Koplik spots, the prodromal rash on mucous membranes such as inside the mouth, are bluish-white against a red background (Figure 2). They confirm the diagnosis for the experienced clinician before the onset of the characteristic morbilliform rash (Figure 3). The rash appears several days after the fever begins and corresponds with the immune response to the infection; it typically spreads from the head down. Extreme malaise is characteristic; in fact, children infected with measles are described as “feeling measly.”

The presentation varies somewhat among certain groups.

Nonimmune pregnant women have an especially severe course, likely related to the relative immune suppression of pregnancy.

In immune-suppressed states, measles is not only more severe, it is also difficult to diagnose because the rash can be absent.

In partially vaccinated children and adults, the disease may present atypically, without cough, conjunctivitis, and coryza, and it may be milder, lacking some of the extreme malaise typical of measles and with a shortened course. Measles infection in people who received the inactivated measles vaccine that was briefly available from 1963 to 1967 is also associated with atypical measles syndrome, a severe hypersensitivity reaction to the measles virus. Atypical measles can be prevented by revaccination with a live-virus vaccine.

DIAGNOSIS MAY NEED TO BE CONFIRMED

The diagnosis of measles is straightforward when all of the signs and symptoms are present. In partially vaccinated populations, however, the diagnosis may need to be confirmed by serologic or polymerase chain reaction (PCR) testing.

Differential diagnosis

The differential diagnosis of the fever and a rash typical of measles in children, especially when accompanied by severe malaise, includes the following:

Kawasaki disease. However, the red eyes of Kawasaki are an injection of the bulbar conjunctivae with sparing of the limbus. No eye exudate is present, and respiratory illness is not part of the disease.

Drug eruptions can present with a morbilliform rash and sometimes fever, but not the other signs of measles in either adults or children.

Scarlet fever has a different rash, the sand-
paper rash typical of toxin-mediated disease.

Rubella tends to cause mild respiratory symptoms and illness rather than the severe disease of measles and other rash-causing viral infections in children and infants.

**Confirmation in confusing cases**

To confirm a diagnosis of measles, samples from throat, nasal, and posterior nasopharyngeal swabs should be collected with a blood specimen for serology and sent to the state public health laboratory. The US Centers for Disease Control and Prevention gives instructions on who should be tested and with which tests.

Most testing now uses PCR for viral RNA, as viral culture is more costly and takes longer. For accurate diagnosis, samples for PCR must be obtained during the acute illness.

The serologic gold standard for diagnosis is a 4-fold rise or fall in immunoglobulin G (IgG) titer of paired serum samples sent 10 days to 2 weeks apart around the illness. The IgM test may be negative initially, and a negative test cannot be used to rule out the diagnosis. Confirmed cases should be reported to public health authorities.

### COMPLICATIONS: EARLY AND LATE

Frequent complications of measles infection include those related to the primary viral infection of respiratory tract mucosal surfaces, as well as bacterial superinfections. Complications are most likely in children under age 5, nonimmune adults, pregnant women, and immunocompromised people. Typical complications include otitis media, laryngotracheobronchitis (presenting as a croupy cough), pneumonia, and diarrhea.

Late sequelae of measles infection are related in part to serious mucosal damage and generalized immune suppression caused by the virus. Even after recovery from acute infection, children can have persistent diarrhea and failure to thrive, with increased mortality risk in the months after infection. Tuberculosis can reactivate in patients already infected, and new tuberculosis infection can be especially severe. Further, tuberculosis skin tests become less reliable immediately after measles infection. Severe disease and fatalities are increased in populations that have baseline vitamin A deficiency and malnutrition.

Death from measles is most often caused by viral pneumonia, secondary bacterial pneumonia, and postviral encephalitis. Before the vaccine era, measles encephalitis occurred in the United States in about 1 in 1,000 measles cases.

Subacute sclerosing panencephalitis is a rare, late, and often fatal complication of measles that presents 7 to 10 years after acute measles infection, usually in adolescence. Beginning with myoclonic jerks, stiffening, and slow mental deterioration, it progresses over 1 to
Measles deaths are most often caused by viral pneumonia, secondary bacterial pneumonia, and postviral encephalitis.

3 years, with a relentless degenerative course leading to death. Since the introduction of the measles vaccine in 1957, this disease has essentially disappeared in the United States.

### SUPPORTIVE CARE, INFECTION CONTROL

Management of measles and its complications is primarily supportive.

**Vitamin A** should be given to all children with acute disease to decrease the risk of complications, including blindness and death (Table 1). Most likely, adults with acute infection should also get vitamin A, though there are no data to support or refute the recommendation in this population.5

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Vitamin A Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children 12 months or older</td>
<td>200,000 IU</td>
</tr>
<tr>
<td>Infants 6–11 months</td>
<td>100,000 IU</td>
</tr>
<tr>
<td>Infants &lt; 6 months</td>
<td>50,000 IU</td>
</tr>
</tbody>
</table>

Another dose is recommended 4–6 weeks after the onset of the acute infection if vitamin A deficiency is likely to be present.

Information from reference 5.

Measles deaths are most often caused by viral pneumonia, secondary bacterial pneumonia, and postviral encephalitis.

TABLE 1

<table>
<thead>
<tr>
<th>Vitamin A for acute measles infection: World Health Organization recommendations</th>
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</thead>
<tbody>
<tr>
<td>Vitamin A once daily for 2 days, at the following doses:</td>
</tr>
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TABLE 2
Measles, mumps, and rubella vaccination: CDC recommendations

<table>
<thead>
<tr>
<th>Patient category</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Routine vaccination</td>
<td>Give 1 dose of measles, mumps, and rubella (MMR) vaccine</td>
</tr>
<tr>
<td>Patient with no evidence of immunity to measles, mumps, or rubella (see Table 3)</td>
<td></td>
</tr>
<tr>
<td>Special situations</td>
<td></td>
</tr>
<tr>
<td>Pregnancy with no evidence of immunity to rubella</td>
<td>MMR is contraindicated during pregnancy</td>
</tr>
<tr>
<td></td>
<td>After pregnancy (before discharge from healthcare facility), give 1 dose of MMR</td>
</tr>
<tr>
<td>Nonpregnant women of childbearing age with no evidence of immunity to rubella</td>
<td>Give 1 dose of MMR</td>
</tr>
<tr>
<td>Human immunodeficiency virus (HIV) infection with CD4 count ≥ 200 cells/μL for at least 6 months and no evidence of immunity to measles, mumps, or rubella</td>
<td>Give 2-dose series of MMR at least 4 weeks apart</td>
</tr>
<tr>
<td></td>
<td>MMR is contraindicated in HIV infection with CD4 count &lt; 200 cells/μL</td>
</tr>
<tr>
<td>Severe immunocompromising conditions</td>
<td>MMR is contraindicated</td>
</tr>
<tr>
<td>Students in postsecondary educational institutions, international travelers, and household or close personal contacts of immunocompromised persons with no evidence of immunity to measles, mumps, or rubella</td>
<td>1 dose MMR if previously received 1 dose MMR, or 2-dose series MMR at least 4 weeks apart if previously did not receive any MMR</td>
</tr>
<tr>
<td>Healthcare personnel born in 1957 or later with no evidence of immunity to measles, mumps, or rubella</td>
<td>2-dose series MMR at least 4 weeks apart for measles or mumps, or at least 1 dose MMR for rubella; if born before 1957, consider 2-dose series MMR at least 4 weeks apart for measles or mumps, or 1 dose MMR for rubella</td>
</tr>
</tbody>
</table>

From the US Centers for Disease Control and Prevention.

RECOMMENDATIONS

In the midst of an outbreak and with rising public awareness of the threat of measles, it is important to recognize that MMR vaccination is the most effective way to prevent spread of the virus and maintain measles elimination in the United States. With this in mind, there are several key facts and recommendations regarding vaccination:

Recommendations on vaccination
- In measles-controlled populations, all children should be vaccinated between 12 and 15 months of age and again before kindergarten.
- In outbreak settings, children should receive a first vaccine dose at 6 months of age, a second at 12 to 15 months of age, and a third before kindergarten.
- Children who have received 2 measles vaccine doses can be assumed to be fully vaccinated and thus protected as long as the first dose was after 12 months of age. If the first dose was before 12 months of age, a child needs 3 doses.
- Adults born before 1957 can be assumed to have had measles infection and to be immune.
- Adults who were immunized with the inactivated measles vaccine available between 1963 and 1967 should receive 1 dose of live virus vaccine.
- Boosters are recommended for young adults who did not receive a second dose of vaccine and for adults with an uncertain history of immunization. There is no need to check titers before giving a booster, but if a positive titer is available in an adult, a booster is not needed.
- Healthcare providers should vaccinate unvaccinated or undervaccinated US residents...
MEASLES

TABLE 3
US Centers for Disease Control and Prevention criteria for evidence of immunity to measles

At least one of the following:

Written documentation of adequate vaccinations including 1 or more doses of measles vaccine given after 12 months of age (preschool-age children) and adults “not at high risk”

Written documentation of 2 doses of vaccine for school-age children and adults at high risk: college students, healthcare personnel, and international travelers

Laboratory evidence of immunity

Laboratory confirmation of measles

Birth before 1957

Information from reference 4.

Give vitamin A to all children with acute disease to decrease the risk of severe disease and complications.

References


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