

RECENT APPROACH IN THE TREATMENT OF MEASLES

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INTRODUCTION

Background:

Measles virus (MV), a negative-enveloped RNA virus, is a member of the Morbillivirus genus in the Paramyxoviridae family. Measles is a highly communicable acute disease marked by prodromal fever, cough, coryza, conjunctivitis, and pathognomonic enanthem (ie, Koplik spots), followed by an erthematous maculopaular rash on the third to seventh day. Infection confers lifelong immunity.

A generalized immunosuppression that follows acute measles frequently predisposes patients to bacterial otitis media and bronchopneumonia. In approximately 0.1% of cases, measles causes acute encephalitis. Subacute sclerosing panencephalitis (SSPE) is a rare chronic degenerative disease that occurs several years after measles infection. Because of a failure to deliver at least 1 dose of measles vaccine to all infants in certain

Industrialized and developing nations, measles remains a common disease in certain regions and is the major infectious cause of mortality worldwide for children younger than 5 years.

Maternal antibodies play a significant role in protection against infection in infants younger than 1 year and may interfere with live-attenuated measles vaccination. A single dose of measles vaccine administered to a child older than 12 months induces protective immunity in 95% of recipients. because MV is highly contagious, a 5% susceptible population is sufficient to sustain periodic outbreaks in otherwise highly vaccinated populations. A second dose of vaccine, now recommended for all school-aged children in the United States, induces.

Immunity in about 95% of the 5% who do not respond to the first dose. Slight genotypic variation in recently circulating strains has not affected the protective efficacy of live-attenuated measles vaccines.

Vitamin A supplementation during acute measles significantly reduces risks of morbidity and mortality.Path.

MV is spread by aerosol and enters the susceptible host by the respiratory route. Initial infection and viral replication occur locally in tracheal and bronchial epithelial cells. After 2-4 days, MV infects local lymphatic tissues, perhaps carried by pulmonary macrophages. Following the amplification of MV in regional lymph nodes, a predominantly cell-associated viremia disseminates the virus to a variety of organs prior to the appearance of rash.

In individuals with deficiencies in cellular immunity, MV causes a progressive and often fatal giant cell pneumonia. Measles causes an immunosuppression marked by decreases in delayed-type hypersensitivity, interleukin-12 production, and antigen-specific

lymphoproliferative responses that persist for weeks to months after the acute infection.

Immunosuppression may predispose individuals to severe bacterial infection, particularly bronchopneumonia, a major cause of measles related mortality among younger children.

Clinical

History: The incubation period from exposure to onset of symptoms ranges from 8-12 days. The prodromal phase is marked by malaise, fever, anorexia, conjunctivitis, cough, and coryza. The entire course of uncomplicated measles, from late prodrome to resolution of fever and rash, is 7-10 days. Cough may be final symptom to appear.

Physical :

- Fever: A temperature exceeding 101°F begins with the prodrome and persists 7-10 days.
- Enanthem: Koplik spots (ie, bluish-gray specks or “grains of sand” on a red base) appear on the buccal mucosa opposite the second molars near the end of the prodrome, just prior to appearance of rash. This enanthem begins to slough as the rash appears.
- Rash : An erythematous and maculopapular rash that becomes confluent begins on the face, then proceeds to the trunk, extremities, palms, and soles and lasts for about 5 days. Patients appear most ill during the first or second day of the rash. Desquamation, which

sparing the palms and soles, may occur after

- 1 week. The rash may be absent in patients with underlying deficiencies in cellular immunity.
- Lymphoid involvement: Generalized lymphadenopathy, mild hepatomegaly, and appendicitis may occur because of generalized involvement of the lymphoid tissues.

Treatment

Medical care:

- Consider administration of antibiotics (if evidence exists of otitis media or bacterial pneumonia) (particularly for children aged 6-24 mo), or ribavirin (experimental).
- To prevent or modify measles in exposed susceptible individuals, consider administering MV human immunoglobulin.

Consultations:

Consult public health or infectious disease specialists for recommendations and guided diagnostic confirmation of cases and prophylaxis of susceptible contacts.

Drug Category

1. Vitamins:-

Vitamin A treatment for children with measles in developing countries has been associated with a marked reduction in morbidity and mortality. The World Health Organization recommends vitamin A administration to all children with measles in communities where vitamin

A deficiency is a recognized problem and where the MV-related mortality rate exceeds 1%. Of note, low serum concentrations of vitamin A are found in children with severe measles in the United States. Thus, consider supplemental Vitamin A in patients aged 6 months to 2 years who are hospitalized with measles and its complications (eg, croup, pneumonia, diarrhea).

● Also consider vitamin A supplementation for any patient who meets the following criteria:

1. Is older than 6 months and has measles
2. Is not already receiving vitamin A supplementation
3. Is immunodeficient
4. Has clinical evidence of vitamin A deficiency
5. Has moderate-to-severe malnutrition
6. Has recently emigrated from an area with high mortality rates due to measles.

Drug Name	Vitamin A (Aquasol A) – Fat—soluble vitamin needed for growth of skin, bones, male and female reproductive organs.
Pediatric Dose	<p><6 months: Not established</p> <p>6 months to 1 year: 100,000 IUPO as a single dose; repeat dose the next day and at 4 wk for ophthalmologic evidence of vitamin A deficiency</p> <p>>1 year: 200.000 IU OP as a single dose;</p>

	repeat dose the next day and at 4 wk for ophthalmologic evidence of vitamin A deficiency
Contraindications	Documented hypersensitivity; large doses may be teratogenic and, thus, contraindicated in pregnancy
Interactions	Cholestyramine or neomycin retard absorption
Precautions	A 200,000IU dose may be associated with Vomiting and headache; patients with hepatic dysfunction have increased susceptibility to vitamin A toxicity

2. Antivirals:-

MV is susceptible to ribavirin in vitro. Although ribavirin (either IV or aerosolized) has been used to treat severely affected and immunocompromised adults with acute measles or SSPE IV (plus intrathecal high-dose interferon-alfa), no controlled trials have been conducted; ribavirin is not approved by the Food and Drug Administration (FDA) for this indication, and such use should be considered experimental

Drug Name	Ribavirin (Virazole)–For experimental use only. A guanosine analog, the mechanism of action is not fully defined but relates to alteration of cellular nucleotide pools and of viral messenger RNA information.
Pediatric Dose	Not established
Contraindications	Documented hypersensitivity
Interactions	Interacts with thymidine-phosphorlated nucleoside analogs (eg, zidovudine, d4T), decreasing effects
Precautions	Closely monitor patients with COPD and asthma for deterioration of respiratory function; associated with a dose dependent hemolytic anemia

3. Vaccines:-

Available in the United States with attenuated rubella and mumps viruses measles-mumps rubella (MMR) vaccine. If administered within 72 hours of exposure to measles, may prevent or attenuate disease. (In a susceptible household contact, consider immunoglobulin instead). Vaccines also are used for universal immunization of children older than 12 months in the United States or at age 9 months in developing countries with high endemicity.

In the United States, a second dose can be administered as soon as 2 months later but is generally administered at age 4-6 years. All adults born after 1957 should receive a second dose of MMR unless they are documented as seropositive for measles IgG antibody by enzyme immunoassay (EIA).

- In the United States, 48 states and the District of Columbia require a second dose of measles vaccine for school enrollment. Rates of seroconversion average 85% after a single dose at age 9 months (the recommended strategy for routine immunization in developing countries), 95% after a single dose at 12 months, 98% after a single dose at age 15 months, and greater than 99% after 2 doses after age 12 months.

Drug Name	Measles virus vaccine (Attenuvax)– For anyone born in or after 1957 who lacks documentation of live vaccine immunization on or after his first birthday.
Pediatric Dose	>12 months: administer as in adults
Contraindications	Documented hypersensitivity; pregnancy; immunodeficiency or immunosuppression (eg, secondary to HIV infection with very low CD4+ T-lymphocyte count, high-dose corticosteroids for .14 d, leukemia)

<p>Interactions</p>	<p>Drug that suppress the immune system may diminish response to immunization; live-attenuated measles vaccines may induce general suppression of cellular immunity that lasts for several wk; therefore, interpretation of purified tuberculin test for tuberculosis infection may be altered (if TB test is indicated, place on day of measles immunization)</p>
<p>Precautions</p>	<p>Contraception in females is advised for 3 mo following immunization</p>

4. Immunoglobulins:-

Human immunoglobulin prevents or modifies measles in susceptible individuals if administered within 6 days of exposure.

<p>Drug Name</p>	<p>Immunoglobulin – Indicated for all susceptible contacts of patients with measles who reside in the same household who are pregnant, immunocompromised, or aged 6-12 mo; also indicated for all children and adolescents with HIV infection who are exposed to measles, regardless of measles immunization status, unless they</p>
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	have received IGIV (400 mg/kg as party of routine immunoprophylaxis) within 3 wk of exposure
Pediatric Dose	0.25 ml/kg IM (0.5 ml/kg for patients with HIV); not to exceed 15 ml/dose
Interactions	May inactivate live virus vaccines (eg, MMR, Varivax); do not administer within 5-6 mo of vaccine
Contraindications	Documented hypersensitivity; IgA deficiency; anti IgE/IgG antibodies
Precautions	Check serum IgA before IVIG (use an IgA-depleted product; eg Gammagard S/D); infusions may increase serum viscosity and thrombotic events; infusions may increase risk of migraine attacks, aseptic meningitis (10%), urticaria, pruritus, or petechiae (2-5 d postinfusion to 30 d); increases risk of renal tubular necrosis in elderly people and in those with diabetes, volume depletion, and preexisting kidney disease; laboratory result changes associated with infusions include elevated antiviral or antibacterial antibody titers for 1 mo, 6-fold

increase in ESR for 2-3 weeks, and apparent hyponatremia.

Further Inpatient Care

- Hospitalization may be indicated for treatment of complications (eg, bacterial superinfection, pneumonia, dehydration, croup).
- Perform timely contact tracing and institute prophylaxis or immunization, if indicated.

Prevention:

- Prevention requires vaccination with live-attenuated measles vaccine (per routine) or earlier immunization (ie, no younger than age 6 mo) during epidemics.
- Human immunoglobulin prevents or modifies disease in susceptible contacts if administered within 6 days of exposure.

Prognosis:

- Most children recover uneventfully. High case-fatality rates may be observed among children who are malnourished or immunodeficient, particularly in developing nations.

A syndrome called atypical measles has been described in individuals who were infected with wild MV several years after immunization with a killed measles vaccine (a vaccine used in the United States from 1963-1967). The disease tends to be more prolonged and severe than regular measles and is marked by a prolonged high fever, pneumonitis, a rash that begins peripherally and may be urticarial, maculopapular, hemorrhagic, and/or vesicular. The assumed pathogenesis is hypersensitivity to MV in a

partially immune host. Laboratory tests reveal a very low measles antibody titer early in the course of the disease, followed soon thereafter by the appearance of an extremely high measles IgG antibody titer (eg, 1:1,000,000) in the serum.

References:

- Technical basic for the case management of measles. WHO/CNR/ EPI/1995- Geneva, World Health Organization, 1995.
- American Academy of Pediatrics: Measles. In: Pickering LK, Red Book: Report of the Committee on Infectious Disease. Elk Grove, Ill: American Academy of Pediatrics; 2000:35-96.
- Centers for Disease Control and Prevention: Measles – United States, 1999. MMWR Morbidity and Mortality Weekly Report June 30, 2000; 49(25): 557-60.
- Centers for Disease Control and Prevention: Global measles control and regional elimination, 1999. MMWR Morbidity and Mortality Weekly Report 1999 Dec 17; 48(49): 1124-30 [Medline].
- Centers for Disease Control and Prevention: Strategies for reducing global measles mortality. --- Epidemiol Rec 2000 Dec 15; 75(50): 411-6 [Medline].
- Gershon AA: Measles virus (rubeola). In : Mandell, Douglas and Bennett's Principles and Practice infectious Diseases. Philadelphia, Pa: Churchill Livingstone; 1995:1519-26.
- Hosoya M, Shigeta S, Mori S: High-dose intravenous ribavirin therapy for subacute sclerosing panencephalitis. Antimicrob Agents Chemother 2001 Mar; 45(3):943-5 [Medline].