Measles

DISEASEDEX™ General or Emergency Medicine Clinical Review

BACKGROUND

Definition

Acute viral disease characterized by fever, cough, rhinitis, and conjunctivitis followed by a maculopapular rash [1]

Epidemiology

United States

In 2000, measles was no longer endemic in the United States (US). The number of measles cases increased from 140 in 2008 to 220 in 2011 and then decreased to 189 in 2013. In the first half of 2014, 16 outbreaks involving 514 cases occurred in 20 states. Forty-eight separate importations occurred. Vaccination status for 506 cases included 81% unvaccinated, 12% status unknown, and 7% vaccinated [1].

Global

From 2000 to 2013, measles incidence decreased 72%, from 146 to 40 cases per million. Annual estimated measles deaths decreased 75%, from 544,200 to 145,700 [1].

Seasonal

In temperate areas, measles occurs mainly in the late winter and spring [1].

Etiology/Pathophysiology

The measles virus is an enveloped RNA virus with 1 serotype. Humans are the only natural host of the measles virus. Measles is one of the most common communicable infectious diseases. It is usually transmitted by direct contact with infectious droplets, but airborne transmission may also occur rarely [1].

Patients are contagious from 4 days before until 4 days after the appearance of the rash. Immunocompromised patients may be contagious for the duration of the illness [1].

The incubation period is usually 8 to 12 days from exposure to onset of symptoms [1].

Complications

- Otitis media
- Pneumonia
- Croup
- Diarrhea
- Viral encephalitis
- Subacute sclerosing panencephalitis

HISTORY AND PHYSICAL

Summary

Symptoms of measles usually occur 8 to 12 days after exposure. The disease is characterized by fever, cough, rhinitis, and conjunctivitis, followed by a maculopapular rash. The rash starts on the face and spreads downward and from the center of the body outward. Koplik spots may appear during the prodromal period. Patients are contagious from 4 days before to 4 days after the appearance of the rash [1].

Medical History

show details

- Foreign travel history finding
- MMR vaccination status
- Occupational Exposure
- Patient immunocompromised
- Nutritional disorder
- Nonspecific lung disease, chronic

Findings

show details

Dermatologic

- Maculopapular eruption

ENT

- Nasal discharge
- Koplik spots

Gastrointestinal

- Diarrhea

General

- Fever

Ophthalmic
- Conjunctivitis
- Photophobia

Respiratory
- Cough

Details

Second Level Medical History Information

Foreign travel history finding

MMR vaccination status

In the United States in the first half of 2014, 16 outbreaks involving 514 cases occurred in 20 states. Vaccination status for 506 cases included 81% unvaccinated, 12% status unknown, and 7% vaccinated [1].

Occupational Exposure

Adults at increased risk for measles include health care workers. Nosocomial transmission of the virus from airborne spread in medical settings, particularly emergency departments, appears to be a significant factor in multiple outbreaks of measles [29][30][31].

Patient immunocompromised

Measles in children and some adults with immune systems impaired by malignant disease, HIV infection, or chemotherapy may present atypically, experience severe disease, and have poorer outcomes. Diagnosis requires a high level of suspicion, especially during an epidemic. In one series, serious complications including pneumonitis and encephalitis developed in 80% of immunocompromised patients; these complications may appear before the illness is recognized as measles [32].

Nutritional disorder

Malnourished or vitamin-A deficient children are at greater risk of severe measles [33][34][35]. In one study, anemia, which may be an indicator of nutritional status, was a risk factor for developing severe measles [5].

Nonspecific lung disease, chronic

Preexisting chronic pulmonary conditions are a risk factor for the development of severe measles [5]. Additionally, a history of respiratory infections is also associated with severe measles [36].

Second Level Finding Information

Dermatologic

Maculopapular eruption

The maculopapular rash is normally preceded by fever, cough, rhinitis, and conjunctivitis. It usually starts on the face and spreads down and from the center out. The rash may be absent in immunocompromised patients [1].

ENT

Nasal discharge

Rhinitis precedes the maculopapular rash[1].

Koplik spots

Koplik spots are an inflammation of the submucosal glands associated with greyish-white specks of sand against an erythematous background on the mucosal membrane opposite the lower molar near the opening of Stenson duct. In children, Koplik spots appear 1 to 2 days before the onset of the rash and disappear 12 to 18 hours later. In adults, Koplik spots often coexist with the rash and persist for at least 3 to 5 days [37].

Gastrointestinal

Diarrhea

Diarrhea is a complication of measles that commonly occurs in young children and immunocompromised patients [1].

General

Fever

Fever precedes the maculopapular rash [1].

Ophthalmic

Conjunctivitis

Conjunctivitis precedes the maculopapular rash [1].

Photophobia

An abnormal intolerance of light is present in the majority of children with measles but rarely occurs in adults [37].

Respiratory

Cough

Cough precedes the maculopapular rash [1].

DIAGNOSTIC TESTING

Diagnostic Testing Summary

Diagnosis of measles virus infection may be made by (1) a positive serologic test result for measles IgM antibody, (2) a significant increase in measles IgG antibody concentration in paired acute and convalescent serum specimens (collected at least 10 days apart) by any standard serologic assay, or (3) identification of measles RNA, preferably specimens from throat or nasopharyngeal secretions [1].

Viral specimens are processed by state public health laboratories or the CDC [1].

Hypocalcemia, hypophosphatemia, and abnormal liver function tests may be associated with measles [2][3][4]. Leukopenia, lymphocytosis, and anemia are possible in measles [5].

Tests

show details

Suspected or known measles exposure [1].[6][7][8] [show details and secondary tests]

Measles antibody level

Strength of Recommendation: Class IIa

Strength of Evidence: Category B

Results

Measle-specific IgM serology is the standard rapid test for laboratory confirmation of measles [1].[7][9][10].

Suspected or known measles [1]. [show details and secondary tests]

Detection of Measles virus using polymerase chain reaction technique

Results

Reverse-transcriptase polymerase chain reaction analysis directly detects measles virus RNA. Throat or nasopharyngeal swabs are preferred [1].

Details

Second Level Test Information

Suspected or known measles exposure [1].[6][7][8]

Measles antibody level

Strength of Recommendation: Class IIa

Strength of Evidence: Category B

Efficacy

In a review of four studies to assess the value of the clinical case definition in areas where the incidence of measles was low, serological confirmation was useful in providing an accurate diagnosis of measles and effectively providing data to identify true cases for disease surveillance. Overall, the sensitivity of clinical case definition to diagnose measles decreased from 88% when the incidence of disease was 171 cases/100,000 population to 76% when the incidence was 64 cases/100,000 population [6].

Accuracy

Sensitivity

In a study of 423 patients with confirmed measles, sera were analyzed using three enzyme immunoassays (EIA); the Meddens EIA (Netherlands) and Denka Seiken (Japan) EIA had a sensitivity of 97%, while the Behring (Germany) EIA had a sensitivity of 88% [8].

Specificity

In a study of 423 patients with confirmed measles, sera were analyzed using three EIAs. The Behring EIA and Denka Seiken EIA had similar specificities of 99% and 98.2%, respectively; Meddens EIA had a specificity of 95% [8].

Positive Predictive Value

In a study of 423 patients with confirmed measles, sera were analyzed using three EIAs. The positive predictive values (PPV) of Behring EIA and Denka Seiken EIA were similar at 99.7% and 99%, respectively. Meddens EIA had a PPV of 97.4% [8].

In areas of low disease prevalence, PPV can decrease significantly. If the prevalence of disease is 50% and the sensitivity is 90%, and the specificity is 99%, the PPV is 99%. However, if the disease prevalence is 1% the PPV drops to 48% [7].

Negative Predictive Value

In a study of 423 patients with confirmed measles, sera were analyzed using three EIAs. The negative predictive value (NPV) of Meddens EIA was 95% followed by Denka Seiken EIA (94.4%), and Behring EIA (89%) [8].

Results

Serology positive

A positive IgM antibody result on a single serum specimen from a person with suspected measles is the simplest method for establishing the diagnosis [1]. IgM enzyme immunoassays (EIAs) are the preferred method to diagnose measles [7][10]. The timing of specimen collection, immunization status of the patient, and the specific assay used affect the sensitivity of the test [1].

IgM assays often are positive on the day of rash onset, but up to 20% of IgM assays may be false negative in the first 72 hours after rash onset. Measles IgM may be detected for at least 1 month after rash onset in unimmunized patients but may be absent or only transiently present in patients immunized with 1 or 2 vaccine doses [1].

To evaluate potential disease exposure an accurate history of vaccination is necessary. IgM antibody response may persist for up to 8 weeks or more after immunization [38].

Negative measurement finding

A negative result does not rule out measles in immunized patients. Measles IgM may be absent or only transiently present in patients who received 1 or 2 vaccine doses [1].

Up to 20% of IgM assays may be false negative in the first 72 hours after rash onset. Obtain a second serum specimen and repeat the IgM test if the initial result is negative and the patient has a generalized rash that lasts more than 72 hours [1].

False Results

False positive results can occur in the presence of rheumatoid factor and occur more frequently with indirect IgM assays. Sera from patients with Epstein-Barr virus, cytomegalovirus, human herpesvirus 6, and mycoplasma have also produced false positive or equivocal results. Attempts to remove these immune complexes have not been successful [7].

False positive results can also occur more frequently when disease prevalence is low. To resolve potential issues surrounding positive IgM results in isolated suspected measle cases, laboratories can use the results generated from IgG EIAs along with IgM results [7].

False negative results have also been reported with IgM assays if the serum sample is collected too early after the first appearance of a clinically suspicious rash [7]. Up to 20% of IgM assays may be false negative in the first 72 hours after rash onset [1].

Suspected or known measles [1].

Detection of Measles virus using polymerase chain reaction technique

Results

Positive measurement finding

Measles may be diagnosed by identification of measles RNA by reverse-transcriptase polymerase chain reaction (PCR) analysis from urine, blood, or throat or nasopharyngeal secretions. Throat or nasopharyngeal swabs are preferred; specimens from more than 1 site may improve results. [1].

Suspected or known measles [5]

Complete blood count

Efficacy

A decreased red blood cell count has been identified as a risk factor for the development of severe measles; it was present in 44% of patients with severe measles in one study [5].

Results

Lymphocytosis

Lymphocytosis is often present in measles.

Leukopenia

Patients with measles often have leukopenia.

Anemia

A hemoglobin of less than 10 g/dL may be secondary to measles infection or a specific nutritional deficiency [5].

Suspected or known measles [2][3][39]

Serum calcium measurement

Results

Hypocalcemia

Transitory, asymptomatic hypocalcemia associated with a decrease in the parathyroid hormone level has been reported during epidemics of measles in nonvaccinated young adults [4][39].

In one series, serum calcium less than 2 mmol/L was present in 54% of hospitalized adults with measles [3].

Hypocalcemia has also been reported in children and may be severe. One series found serum calcium levels less than 1.87 mmol/L in 11 of 15 children with severe measles. Phosphorus levels were normal to low, suggesting decreased absorption or malnutrition rather than hypoparathyroidism [2].

Suspected and known measles [3][40][37]

Hepatic function panel

Results

Abnormal finding on evaluation procedure

Transient impairment of liver function has been reported in over 70% of adults with measles, indicating that subclinical hepatitis is a characteristic manifestation rather than a complication in this age group [40][37][4].

Serum aspartate aminotransferase, alanine aminotransferase, and lactate dehydrogenase levels greater than 5 times normal have been described in hospitalized adults with measles [3].

DIAGNOSIS

Diagnostic Criteria

show details

- Centers for Disease Control

Differential Diagnosis

- Scarlet fever
- Adverse reaction to drug

- Erythema multiforme
- Disease due to Enterovirus
- Rocky Mountain spotted fever
- Rubella
- Roseolar erythema
- Primate erythroparvovirus 1 infection
- Cytomegalovirus infection
- Leptospirosis
- Pityriasis rosea

Details

Second Level Diagnostic Criteria

Centers for Disease Control

[27]

- A clinical case of measles is characterized by all of the following:
  - A generalized rash lasting 3 or more days
  - Fever
  - Cough, rhinitis, or conjunctivitis
- Probable measles is diagnosed if the following criteria are met:
  - The clinical case definition is met
  - The illness is not epidemiologically linked to a laboratory confirmed case
  - The illness has noncontributory or no serologic or virologic testing
- Confirmed measles is diagnosed if one of the following criteria are met:
  - The case meets the laboratory criteria for measles, consisting of one of the following:
    - A positive serologic test for measles IgM antibody
    - A significant rise in measles antibody level by any standard serologic assay
    - Isolation of measles virus from a clinical specimen
  - The case meets the clinical case definition and also is epidemiologically linked to a laboratory confirmed case.

TREATMENT

Treatment Summary

Standard and airborne transmission precautions are recommended in outpatient [11][12][13] and inpatient settings in patients with measles illness and exposed susceptible patients [1].

Report all cases of suspected measles to the local or state health department immediately, without waiting for diagnostic test results [1].

Specific antiviral therapy for measles is not available. Vitamin A is recommended by WHO for

all children with acute measles, regardless of country of residence [1].

Consider measles vaccine in all exposed persons who are vaccine-eligible and have not been vaccinated or have received only 1 dose of vaccine [1].

IG given within 6 days of exposure may prevent or modify measles if measles immunity is not evident. IG may be administered IV or IM; IV is preferred for pregnant women without evidence of measles immunity and for individuals who are severely immunocompromised [1].

Drug Therapy

- **A Vitamins**
  Vitamin A is recommended by WHO for all children with acute measles, regardless of country of residence. It has been associated with decreased morbidity rates in developing countries [1] and a significant reduction in mortality in both hospitalized and nonhospitalized children [14][15]. In the United States, lower vitamin A concentrations were found in children with more severe measles illness [1].
  - In the United States, consideration should be given to vitamin A supplementation in selected cases [14]:
    - Children aged 6 months to 2 years hospitalized with measles and its complications (eg, croup, pneumonia, diarrhea); limited data are available regarding safety and need for vitamin A supplementation for infants less than 6 months of age
    - Children older than 6 months of age with measles who have any of the following risk factors and who are not already receiving vitamin A:
      - Immunodeficiency (eg, acquired, congenital, immunosuppressive therapy)
      - Ophthalmologic evidence of vitamin A deficiency (night blindness, Bitot's spots, xerophthalmia)
      - Impaired intestinal absorption (eg, biliary obstruction, short bowel syndrome, cystic fibrosis)
      - Moderate to severe malnutrition, including that associated with eating disorders
      - Recent immigration from areas with high measles-related mortality
- **Vaccines**
  Postexposure Prophylaxis

  Consider measles vaccine in all exposed persons who are vaccine-eligible and have not been vaccinated or have received only 1 dose of vaccine. Measles vaccine given within 72 hours of exposure may prevent illness or reduce the severity of symptoms [1].

  For children who receive immune globulin (0.5 mL/kg) after measles exposure, administer measles vaccine 6 months after immune globulin administration to children 12 months or older [1].
- **Immune Serums**
  Immune Globulin

  Immune globulin can prevent or modify measles in susceptible persons if given within 6

days of exposure, but is not recommended for close contacts who received 1 vaccine dose at 12 months or older unless they are severely immunocompromised [1].

- IV immune globulin is the recommended preparation for the following patients at higher risk of severe measles and complications [1]:
  - Pregnant women without evidence of measles immunity
  - Severely immunocompromised persons regardless of immunologic or vaccination status, including those with severe primary immunodeficiency
  - Bone transplant recipients until at least 12 months after completion of all immunosuppressive therapy; longer in patients with graft-versus-host disease
  - Acute lymphocytic leukemia patients within and until at least 6 months after completion of immunosuppressive chemotherapy
  - HIV or AIDS patients with severe immunosuppression (CD4+ T cells less than 15% for all ages; CD4+ T cells less than 200/mm^3 in patients older than 5 years) or who have not received vaccination since receiving effective antiretroviral therapy; some experts recommend IV immune globulin prophylaxis for all HIV patients, regardless of immune status or vaccination history

show details

All children with measles, regardless of country of residence (WHO recommendation) [1] or select children with measles in the United States [14] [show details and secondary therapies]

Vitamin A

Pediatrics (Younger than 6 months) 50,000 international units orally or IM once daily for 2 days; give a third dose 2 to 4 weeks later if patient has signs/symptoms of vitamin A deficiency [1]

Pediatrics (6 to 11 months) 100,000 international units orally or IM once daily for 2 days; give a third dose 2 to 4 weeks later if patient has signs/symptoms of vitamin A deficiency [1]

Pediatrics (12 months or older) 200,000 international units orally or IM once daily for 2 days; give a third dose 2 to 4 weeks later if patient has signs/symptoms of vitamin A deficiency [1]

All exposed persons who are vaccine-eligible and have not been vaccinated or have received only 1 dose of vaccine [1][show details and secondary therapies]

Measles Virus Vaccine, Live

Postexposure measles prophylaxis [16][1] within 6 days of exposure in persons without evidence of measles immunity [1][show details and secondary therapies]

Immune Globulin

Adult (Gamastan(R) S/D), persons without evidence of measles immunity) 0.25 mL/kg IM within 6 days of exposure (manufacturer dose) [17]

Adult (persons without evidence of measles immunity) 0.5 mL/kg IM; MAX 15 mL (guideline dose) [18]

Adult (pregnant women without evidence of measles immunity) 400 mg/kg IV (guideline dose) [18]

Adult (severely immunocompromised patients regardless of measles immunity) 400 mg/kg IV (guideline dose) [18]

Pediatrics (persons without evidence of measles immunity) 0.5 mL/kg IM; MAX 15 mL (guideline dose) [18]

Pediatrics (severely immunocompromised patients regardless of measles immunity) 400 mg/kg IV (guideline dose) [18]

Procedural Therapy

show details

Suspected or known measles [1].[19][11][20] [show details and secondary therapies]

Isolation technique

Results

Standard and airborne transmission precautions are recommended in outpatient [11][12][13] and inpatient settings in patients with measles and exposed susceptible patients [1].

Reportable infectious diseases [21][22][23][24][25] [show details and secondary therapies]

Infectious disease notification

Strength of Recommendation: Class I

Strength of Evidence: Category C

Results

In the United States, specific infectious diseases must be reported to the state or local public health departments [21][22][24].

Details

Second Level Drug Therapy

All children with measles, regardless of country of residence (WHO recommendation) [1] or select children with measles in the United States [14]

VITAMIN A (Related toxicological information in VITAMIN A)

Dosing

Pediatrics (Younger than 6 months) 50,000 international units orally or IM once daily for 2 days; give a third dose 2 to 4 weeks later if patient has signs/symptoms of vitamin A deficiency [1]

Pediatrics (6 to 11 months) 100,000 international units orally or IM once daily for 2 days; give a third dose 2 to 4 weeks later if patient has signs/symptoms of vitamin A deficiency [1]

Pediatrics (12 months or older) 200,000 international units orally or IM once daily for 2 days; give a third dose 2 to 4 weeks later if patient has signs/symptoms of vitamin A deficiency [1]

Adverse Effects

Hematologic Effects
- Anemia
- Blood coagulation disorder
- Hematology finding
- Neutropenia

Neurologic Effects
- Neurological finding
- Pseudotumor cerebri

Endocrine Metabolic Effects
- Hypervitaminosis A

Gastrointestinal Effects
- Gastrointestinal tract finding
- Gingivitis

Hepatic Effects
- Abnormal vascular flow
- Cirrhosis of liver
- Hepatic fibrosis
- Hepatotoxicity
- Liver finding

Ophthalmic Effects
- Diplopia

- Eye / vision finding

Respiratory Effects

- Dyspnea
- Respiratory finding

Dermatologic Effects

- Alopecia
- Atopic dermatitis
- Discoloration of skin
- Eczema
- Erythema
- Skin finding

Musculoskeletal Effects

- Musculoskeletal finding
- Osteoporosis
- Osteosclerosis

Immunologic Effects

- Anaphylaxis

Psychiatric Effects

- Psychiatric sign or symptom

Other Therapeutic Adverse Effects

- Genetic mutation

Warnings and Precautions

single oral doses over 25,000 units/kg can cause acute toxicity

evaluate vitamin A intake from fortified foods, dietary supplements, and other concomitant drugs before prescribing

Contraindications

hypersensitivity to vitamin A products

pregnancy (dosages in excess of RDA)

hypervitaminosis A

All exposed persons who are vaccine-eligible and have not been vaccinated or have received only 1 dose of vaccine [1]

MEASLES VIRUS VACCINE, LIVE

Adverse Effects

Hematologic Effects
- Thrombocytopenia

Neurologic Effects
- Aseptic meningitis
- Ataxia
- Dizziness
- Encephalitis
- Encephalopathy
- Febrile seizure
- Guillain-Barre syndrome
- Headache
- Hemiplegia
- Myelitis
- Neurological finding
- Seizure

Endocrine Metabolic Effects
- Increased body temperature

Gastrointestinal Effects
- Diarrhea
- Gastrointestinal tract finding

Respiratory Effects
- Respiratory finding

Dermatologic Effects
- Rash
- Skin finding
- Stevens-Johnson syndrome

Immunologic Effects
- Anaphylaxis
- Hypersensitivity reaction

Otic Effects
- Ototoxicity

Other Therapeutic Adverse Effects
- Adverse reaction to drug
- Death
- Fever

Warnings and Precautions

Active, untreated tuberculosis[41]

Defer vaccination for at least 3 months following blood or plasma transfusions, or administration of immune globulin [41]

Fever may occur following vaccination [41]

History of cerebral injury, individual or family history of convulsions, or any condition in which stress due to fever should be avoided [41]

HIV-infected patients[41]

Hypersensitivity to eggs[41]

Special care should be taken to ensure that the injection does not enter a blood vessel [41]

Temporary depression of tuberculin skin test sensitivity[41]

Thrombocytopenia (may exacerbate condition)[41]

Contraindications

Blood dyscrasias, leukemia, lymphomas, malignant neoplasms of bone or lymphatics [41]

Congenital or hereditary immunodeficiency, family history of (immune competence of potential vaccine recipient must be determined) [41]

Febrile illness, severe [41]

History of anaphylaxis to neomycin[41]

Hypersensitivity to any component of the vaccine, including gelatin [41]

Immunodeficiency states, primary and acquired (cellular immune deficiencies, hypogammaglobulinemia, dysgammaglobulinemia) [41]

Immunosuppressive therapy (does not apply to corticosteroid replacement therapy) [41]

Malignant neoplasms of the bone marrow or lymphatic system

Pregnancy[41]

Pregnancy should be avoided for 28 days postvaccination based on Advisory Committee on Immunization Practices (ACIP) recommendations [42]; pregnancy should be avoided

for 3 months postvaccination based on manufacturer recommendations [41]

[41]

Postexposure measles prophylaxis [16][1] within 6 days of exposure in persons without evidence of measles immunity [1]

IMMUNE GLOBULIN

Dosing

Adult (Gamastan(R) S/D), persons without evidence of measles immunity) 0.25 mL/kg IM within 6 days of exposure (manufacturer dose) [17]

Adult (persons without evidence of measles immunity) 0.5 mL/kg IM; MAX 15 mL (guideline dose) [18]

Adult (pregnant women without evidence of measles immunity) 400 mg/kg IV (guideline dose) [18]

Adult (severely immunocompromised patients regardless of measles immunity) 400 mg/kg IV (guideline dose) [18]

Pediatrics (persons without evidence of measles immunity) 0.5 mL/kg IM; MAX 15 mL (guideline dose) [18]

Pediatrics (severely immunocompromised patients regardless of measles immunity) 400 mg/kg IV (guideline dose) [18]

Adverse Effects

Hematologic Effects

- Anemia
- Direct Coombs test positive
- Ecchymosis
- Hemolysis
- Hemolytic anemia
- Hemorrhage
- Leukopenia
- Neutropenia
- Pancytopenia
- Purpura
- Thrombosis

Cardiovascular Effects

- Angina pectoris
- Cardiac arrest
- Chest discomfort

- Chest pain
- Decreased heart rate
- Heart murmur
- Hypertension
- Hypotension
- Increased blood pressure
- Increased heart rate
- Increased systolic arterial pressure
- Myocardial infarction
- Peripheral edema
- Shock
- Tachycardia

Neurologic Effects

- Aseptic meningitis
- Asthenia
- Cerebrovascular accident
- Coma
- Creutzfeldt-Jakob disease
- Dizziness
- Encephalopathy
- Headache
- Insomnia
- Lethargy
- Loss of consciousness
- Migraine
- Paresthesia
- Posterior reversible encephalopathy syndrome
- Seizure
- Tremor
- Variant Creutzfeldt-Jakob disease

Endocrine Metabolic Effects

- Hypernatremia
- Hyperproteinemia
- Hyponatremia
- Hypothermia
- Increased body temperature
- Pseudohyponatremia

Gastrointestinal Effects

- Abdominal pain
- Aphthous ulcer of mouth
- Diarrhea
- Disorder of gastrointestinal tract
- Gastritis
- Gastroesophageal reflux disease
- Indigestion

- Nausea
- Stomach ache
- Toothache
- Upper abdominal pain
- Vomiting

Renal Effects

- Acute renal failure
- Dysuria
- Glycosuria
- Hypokalemic nephropathy
- Urinary tract infectious disease

Hepatic Effects

- Alkaline phosphatase raised
- ALT/SGPT level raised
- Aspartate aminotransferase serum level raised
- Decreased liver function
- Deficiency of alkaline phosphatase
- Fulminant hepatitis
- Hepatitis B
- Hepatitis C

Ophthalmic Effects

- Blurred vision
- Conjunctivitis
- Uveitis

Respiratory Effects

- Acute lung injury during and following administration of blood product
- Acute respiratory distress syndrome
- Apnea
- Asthma
- Bleeding from nose
- Cough
- Cyanosis
- Dyspnea
- Hypoxemia
- Nasal congestion
- Nasal discharge
- Pain in throat
- Pharyngitis
- Pharyngolaryngitis
- Postnasal drip
- Pulmonary edema
- Pulmonary embolism
- Respiratory crackles
- Respiratory distress

- Respiratory tract congestion
- Sinus headache
- Sinusitis
- Tonsillar adenitis
- Upper respiratory infection
- Wheezing

Dermatologic Effects

- Alopecia
- Atopic dermatitis
- Bullous dermatosis
- Contusion
- Dry skin
- Eczema
- Epidermolysis bullosa
- Erythema at injection site
- Erythema multiforme
- Erythematous rash
- Flushing
- Hematoma
- Injection site edema
- Injection site hemorrhage
- Injection site inflammation
- Injection site irritation
- Injection site pain
- Injection site pruritus
- Injection site reaction
- Petechiae
- Pruritus
- Rash
- Stevens-Johnson syndrome
- Swelling at injection site
- Urticaria

Musculoskeletal Effects

- Arthralgia
- Backache
- Muscle weakness
- Myalgia
- Neck pain
- Pain in limb
- Spasm

Immunologic Effects

- AIDS
- Anaphylaxis
- Complication of infusion
- Hypersensitivity reaction

- Lymphadenopathy

Psychiatric Effects

- Agitation
- Anxiety

Otic Effects

- Acute otitis media
- Otalgia

Other Therapeutic Adverse Effects

- Angioedema
- Dehydration
- Fatigue
- Fever
- Influenza
- Influenza-like illness
- Malaise
- Pain
- Rigor
- Shivering

Warnings and Precautions

Administration: SubQ administration not recommended for idiopathic thrombocytopenic purpura due to increased hematoma risk [43][44].

Administration: Do not inadvertently infuse subQ formulation due to increased risk of thrombotic events [45].

Administration: Inject Gamastan(R) IM only; IV administration may lead to serious adverse reactions [46]

Cardiovascular: Elevations of systolic blood pressure to 180 mm Hg or greater and/or of diastolic blood pressure to 120 mm Hg or greater (hypertensive urgency) have been reported, especially in patients with a history of hypertension; monitoring recommended [47]

Dosing: Expanded fluid volume may cause overload with high-dose regimens [48][43][44][49] for chronic idiopathic thrombocytopenic purpura in patients at increased risk of acute kidney injury, hemolysis, thrombosis, or volume overload [49].

Endocrine and metabolic: Falsely elevated glucose measurements may occur during therapy in diabetic patients because of the maltose ingredient; this increases the risk of masked hypoglycemic episodes and over administration of insulin, potentially causing life-threatening hypoglycemia; monitor blood glucose during therapy with glucose-specific methods in diabetic patients [50].

Endocrine and metabolic: Hyperproteinemia, increased serum viscosity, and hyponatremia may occur; distinguish hyponatremia from pseudohyponatremia (decreased calculated serum osmolality or elevated osmolar gap) [50][51][52][48][43][53][49][54][44].

Endocrine and metabolic: Hyperproteinemia, increased serum viscosity, hypernatremia, or pseudohyponatremia (after sodium level alterations) may occur with Gammagard S/D due to amount of sodium in product [55].

Hematologic: Hemolysis and delayed hemolytic anemia may occur; severe hemolysis-related renal dysfunction, renal failure, and disseminated intravascular coagulation have been reported; increased risk with high doses (2 g/kg or greater), non-O blood group, and underlying inflammation; monitoring recommended [56][57][50][51][52][58][48][43][53][54][44], especially in patients with preexisting anemia or cardiovascular or pulmonary compromise [47].

Immunologic: Do not perform intradermal skin testing to determine hypersensitivity; local tissue irritation may be mistaken for a positive reaction [46]

Immunologic: Use caution in patients with a history of prior systemic allergic reactions following the administration of human immunoglobulin [46]

Immunologic: Severe hypersensitivity reactions have been reported; increased risk in IgA deficiency with anti-IgA antibodies or corn allergy; discontinue use if condition occurs [56][57][50][51][52][48][43][53][54][49][44][59].

Immunologic: Severe hypersensitivity reactions and anaphylactic reactions, with a decrease in blood pressure, have been reported, even in patients that tolerated previous treatments; discontinue use if conditions occur [55]

Immunologic: Infusion reactions (ie, fever, chills, nausea, and vomiting) may occur, especially with first dose or with treatment hiatus of more than 8 weeks; monitoring and adherence to dose and administration guidelines recommended [51][52].

Immunologic: Infectious agent transmission may occur, including viruses and theoretical risk of Creutzfeldt-Jakob disease, as well as unknown or emerging viruses and other pathogens [46][56][57][50][51][52][58][48][43][53][54][49][44][59].

Neurologic: Aseptic meningitis syndrome (AMS) may occur; increased risk with high doses (1 to 2 g/kg or greater) or rapid infusion; discontinuation may be necessary [56][57][50][51][52][58][48][43][53][54][49][44]; increased susceptibility to AMS may occur in patients with migraine history[50] or in female patients [55][56].

Renal: Acute renal dysfunction, renal failure, acute tubular necrosis, proximal tubular nephropathy, osmotic nephrosis, and death may occur with immune globulin products, especially those that contain sucrose; dosage adjustment may be necessary and monitoring recommended, particularly in patients with increased risk (eg, developing renal dysfunction, preexisting renal insufficiency, diabetes mellitus, volume depletion,

sepsis, paraproteinemia, concomitant nephrotic drugs, or patients over 65 years) [56] [57]. If renal function deteriorates, consider discontinuation [47]

Respiratory: Transfusion-related acute lung injury (noncardiogenic pulmonary edema) may occur, usually with presenting symptoms within 1 to 6 hours of treatment; monitoring recommended [56][57][50][51][52][58][48][43][53][54][49][44].

Contraindications

Anaphylaxis or severe systemic reaction to human immunoglobulins [46][56][50][51] [52][58][48][43][53][54][49] or to any component of the product [44], including polysorbate 80 [57]

Hereditary intolerance to fructose, including infants and neonates for whom sucrose or fructose tolerance has not been established [48]

Hyperprolinemia (type I or II); Hizentra(R) and Privigen(R) contain the stabilizer L-proline [57][49]

IgA deficiency with antibodies against IgA, and a history of hypersensitivity [46]; IG products contain trace amounts of IgA [56][57][50][51][52][48][43][53][54][49][44]

Severe thrombocytopenia or any coagulation disorder which would contraindicate IM injections [59]

Second Level Procedural Therapy

Suspected or known measles [1].[19][11][20]

Isolation technique

Technique

Inpatient

Direct contact with infectious droplets is the most common type of transmission of measles; airborne spread is less common. In addition to standard precautions, airborne precautions are recommended for 4 days after rash onset in otherwise healthy pediatric patients and for the duration of illness in immunocompromised patients. Airborne precautions are also recommended for exposed susceptible patients from day 5 after first exposure until day 21 after last exposure [1].

Outpatient

Nosocomial transmission of measles in medical facilities is a significant factor in multiple outbreaks. Measures to reduce the risk of airborne transmission in outpatient settings include respiratory isolation, prompt care of all suspected cases, scheduling

patients with suspected measles for a time of day when fewer or no patients are expected to be present, and ensuring adequate fresh-air ventilation in the facility [11][12][13].

Efficacy

Patients with measles are highly infectious and require isolation as 90% of susceptible household contacts will develop measles [11].

Timing

Children should be kept out of school or daycare for at least 4 days after the appearance of the rash [20].

Infected heath care workers should be excluded from duty for 7 days after the appearance of the rash [19].

Susceptible health care workers exposed to measles should be excluded from duty from the fifth day after the first exposure through the 21st day after the last exposure [19].

Reportable infectious diseases [21][22][23][24][25]

Infectious disease notification

Strength of Recommendation: Class I

Strength of Evidence: Category C

Results

- Infectious diseases in the United States that require health department notification:
  - Acquired Immunodeficiency Syndrome (AIDS) [22]
  - Anthrax [24]
  - Avian influenza A [25]
  - Botulism [24]
  - Brucellosis [24]
  - Chancroid [22]
  - Chlamydia trachomatis, genital infection [22]
  - Cholera [24]
  - Coccidioidomycosis [24]
  - Cryptosporidiosis [24]
  - Cyclosporiasis [24]
  - Diphtheria [24]
  - Dengue [23]
  - Ehrlichiosis, Human Granulocytic [24]
  - Ehrlichiosis, Human Monocytic [24]
  - Ehrlichiosis, Human, other or unspecified agent[24]

- Encephalitis/Meningitis, Arboviral, California serogroup [24]
- Encephalitis/Meningitis, Arboviral, Eastern equine[24]
- Encephalitis/Meningitis, Arboviral, Powassan [24]
- Encephalitis/Meningitis, Arboviral, St. Louis [24]
- Encephalitis/Meningitis, Arboviral, West Nile[24]
- Encephalitis/Meningitis, Arboviral, Western equine [24]
- Giardiasis [24]
- Gonorrhea [22]
- Haemophilus influenzae, invasive disease[24]
- Hansen Disease (leprosy) [24]
- Hantavirus Pulmonary Syndrome[24]
- Hemolytic Uremic Syndrome, postdiarrheal [24]
- Hepatitis, viral [24]
- Hepatitis A, acute [24]
- Hepatitis B, acute [24]
- Hepatitis B, chronic [24]
- Hepatitis B virus, perinatal infection [24]
- Hepatitis C, acute [24]
- Hepatitis C virus, past or present [24]
- Human Immunodeficiency Virus (HIV) infection [22]
- Influenza-associated pediatric mortality [24]
- Legionellosis [24]
- Listeriosis [24]
- Lyme Disease [24]
- Malaria [24]
- Measles [24]
- Meningococcal disease, invasive[24]
- Mumps [24]
- Pertussis [24]
- Plague[24]
- Poliomyelitis, paralytic [24]
- Psittacosis [24]
- Q Fever[24]
- Rabies, animal or human[24]
- Rocky Mountain Spotted Fever[24]
- Rubella, infectious or congenital [24]
- Salmonellosis[24]
- Severe Acute Respiratory Syndrome-associated Coronavirus (SARS-CoV) disease[24]
- Shiga toxin-producing Escherichia coli (STEC) [24]
- Shigellosis[24]
- Smallpox[24]
- Streptococcal disease, invasive, Group A[24]
- Streptococcal Toxic-Shock Syndrome [24]
- Streptococcus pneumoniae, invasive disease, age <5 years[24]
- Streptococcus pneumoniae, invasive disease, drug resistant, all ages [24]
- Syphilis [22]
- Syphilis, Congenital [22]

- Tetanus [24]
- Toxic-Shock Syndrome (other than streptococcal) [24]
- Trichinellosis[24]
- Tuberculosis [24]
- Tularemia[24]
- Typhoid Fever [24]
- Vancomycin-resistant Staphylococcus aureus infection (VRSA)[24]
- Varicella, infection (morbidity)[24]
- Varicella (mortality) [24]
- Yellow fever[24]
- Zika virus disease [21]

Requirements for reporting sexually transmitted diseases other than those listed above varies from state to state. Providers should be aware of reporting requirements applicable within their state of practice [22].

PROGNOSIS

Mortality

Since 2000, death has occurred in 1 to 3 of every 1000 cases reported in the United States. Cause of death was mainly respiratory and neurologic complications. Mortality increased in children younger than 5 years and children who were immunocompromised [1].

From 2000 to 2013, annual estimated measles deaths worldwide decreased 75%, from 544,200 to 145,700 [1].

Pregnancy

Contracting measles during pregnancy may lead to fatal maternal and fetal complications [26]. The most common complications are premature labor, moderately increased rates of spontaneous abortion, and low birth weights [27][28][26].

RELATED INFORMATION

Conditions

- Adverse reaction to drug
- Croup
- Cytomegalovirus infection
- Erythema multiforme
- Measles
- Measles - Prevention & Screening (Clinical Checklist™)
- Otitis media
- Primate erythroparvovirus 1 infection

- Rocky Mountain spotted fever
- Rubella
- Viral encephalitis

Tests & Procedures

- Measles antibody level
- Serum calcium measurement

Drugs

- IMMUNE GLOBULIN
- MEASLES VIRUS VACCINE, LIVE
- VITAMIN A

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