MEASLES: SYMPTOMATIC PATIENT

(Age < 25 years)



Aim: To standardize management of patients with suspected/confirmed measles infection.

Patient with confirmed measles OR symptoms suspicious for measles (see testing algorithm pages 6–7 for detail of whom to test)

- Mask patient + others present (e.g., caregiver, siblings)
- Isolate in an airborne infection isolation room (AIIR; negative pressure). If AIIR is not available, isolate in private room with door closed; patient (+ others) should remain masked.
- Order Airborne Precautions
- Notify Infection Prevention and Control (Amion or 952-260-9021 if at Children's MN); available 24/7

MEASLES SIGNS/SYMPTOMS

- Prodrome (~2–4 days): fever, malaise, and anorexia, followed by conjunctivitis, coryza, and cough.
- Enanthem (~48 hr before rash, NOT seen in all patients): Koplik spots which are 1–3 mm white/gray/bluish elevations with an erythematous base ("grains of salt on a red background") on buccal mucosa or palate.
- Exanthem (2–4 days after fever):
 erythematous, maculopapular,
 blanching rash, which classically
 begins on the face and spreads
 down. Begin as blanching then don't
 blanch. Rash may not appear in
 immunocompromised patients.
- Fever beyond the third to fourth day of rash may suggest a measles-associated complication (note 5).

EXCLUSION GUIDELINES

Patients excluded from this guideline:

Pregnant patients

Obtain history and perform exam

Vaccine status (specify MMR), contacts/exposures (note 1), travel history. Signs/symptoms (including date of rash onset), vital signs, hydration, respiratory status. Consider also alternate etiologies for illness (note 2).

Assess level of illness (note 3)

Mild

Symptomatic but not needing hospitalization for support.

- Obtain labs: "Measles for Suspected Disease (Rubeola) to MDH" in Cerner, "MEASLES PCR to MDH (UMSP)" in eCW.
- Give vitamin A (note 4).
- Evaluate/treat suspected coinfections based on symptoms (note 5).

Discuss with parent/caregiver the need for exclusion from school/daycare for other household members who have not received at least one MMR. See follow-up notes on page 4.

Moderate/Severe

Signs or symptoms requiring hospital admission. Refer to Children's Minnesota ED for evaluation if in clinic (612-343-2121).

- Consider ID consult if questions about clinical management.
 Other specialists if indicated (e.g., ophthalmology if significant eye findings beyond conjunctivitis).
- Obtain labs: "Measles for Suspected Disease (Rubeola) to MDH," CBC+diff, CRP, CMP, and serum to save (≥ 3 mL).
- Give vitamin A (note 4).
- Hydrate with IV fluids if indicated and/or consider NG tube if oral lesions preventing PO intake.
- 2-view CXR if respiratory symptoms to evaluate for infiltrate.
- Evaluate/treat suspected coinfections per symptoms (note 5)
 Antibiotics per suspected sepsis orderset if sepsis is present.

MEASLES: SYMPTOMATIC PATIENT

(Age < 25 years)



NOTE 1

Aim: To standardize management of patients with suspected/confirmed measles infection.

Contact/exposure factors: Incubation period for measles is 6 to 21 days (median 13 days). Period of contagiousness is ~5 days before the appearance of rash to ~4 days afterward.

NOTE 2

Differential diagnosis of measles: Broad, includes for example viruses (enteroviruses, adenovirus, COVID-19, etc.), Rocky Mountain Spotted Fever, scarlet fever, toxic shock, meningococcemia, HSP, Kawasaki Disease, mono, MIS-C, etc.

NOTE 3

Severity of illness levels

- Mild: No respiratory distress or oxygen requirement; able to self-hydrate (may be after initial fluid support).
- Moderate: Requiring ongoing IVF support OR requiring respiratory support including low flow nasal cannula for hypoxia or HFNC for increased WOB.
- Severe: Hypoxia or work of breathing requiring non-invasive or invasive ventilation or concern that patient status is worsening on high flow nasal cannula OR SIRS/Sepsis/Shock OR rapidly worsening.

NOTE 4

Vitamin A is recommended for all patients with measles regardless of nutritional status or country of origin *unless extreme vitamin A supplementation has recently been given.* As measles can decrease serum vitamin A (retinol) levels, checking levels before treatment is not recommended.

- Infants < 6 months: Enteral: 50,000 units/day (15,000 mcg RAE/day) for 2 days.
- Infants 6 to 11 months: Enteral: 100,000 units/day (30,000 mcg RAE/day) for 2 days.
- Children ≥ 12 months: Enteral: 200,000 units/day (60,000 mcg RAE/day) for 2 days.
- If severe malnutrition or ophthalmologic evidence of vitamin A deficiency is present, administer a third dose 2–4 weeks after the 2nd dose.

Unfortunately vitamin A comes in softgel capsules. Children with measles who are not requiring hospitalization should be prescribed vitamin A at the above dosing if they can swallow capsules (note: this may be up to 25 capsules to achieve the required dose). If the child cannot swallow capsules and the pharmacy (e.g., outpatient pharmacy) is unable to draw up sufficient dose effectively, then the provider may defer on vitamin A prescription. All hospitalized patients should receive vitamin A regardless of ability to swallow capsules.

NOTE 5

Acute complications from measles

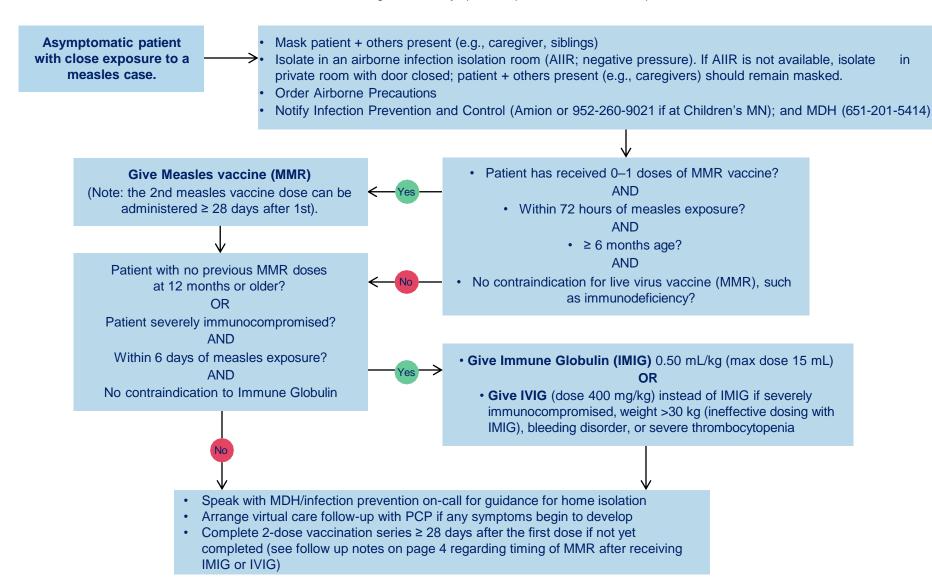
- GI: Diarrhea and stomatitis are common and may lead to poor PO and dehydration.
- Neuro: Encephalitis (~ day 5), acute disseminated encephalomyelitis (~week 2).
- ENT/Resp: Otitis media, tracheitis, croup, and respiratory distress are well-described. Measles pneumonia may cause symptoms and radiographic findings that overlap with bacterial pneumonia. However, co-infections may occur including with Strep pneumoniae,
- Strep pyogenes, H. influenzae, Staph aureus and viruses. Use antibiotics if strong suspicion for a pneumonic bacterial process due to both clinical exam and imaging findings. Utilize age appropriate guideline for work up and empiric treatment of suspected bacterial pneumonia ("Fever without obvious source infant 1-60 days," "Community acquired pneumonia guideline," or "Empiric antibiotic recs for patients ≥18 and <25 years old with common infections"). CXR findings for measles includes: mixed reticular opacities, air space consolidation, and hilar lymph node enlargement.
- Ophthalmology: Purulent conjunctivitis, keratitis, xerophthalmia (risk of blindness). Evaluate for pain, photophobia, erosion, or opacity.

MEASLES: ASYMPTOMATIC PATIENT WITH HIGH-RISK EXPOSURE



(Age < 25 years)

Aim: To standardize management for asymptomatic patients with measles exposure.







Aim: To standardize management for asymptomatic patients with measles exposure.

FOLLOW-UP NOTES

Follow-up should be with PCP within 1-2 days of diagnosis (if managed as outpatient) or discharge (if hospitalized).

- · Consider use of virtual care visits if applicable.
- Assess hydration status. Consider use of Gastroenteritis "Oral Rehydration Therapy" guideline, with patient instructions available on Clinical Guidelines website including in multiple languages.
- Complete 2-dose MMR vaccination series ≥ 28 days after the first dose if not yet completed. See note below regarding timing of MMR after receiving IMIG or IVIG.

Later complications from measles

- **Neuro:** Acute disseminated encephalomyelitis (~ week 2) and subacute sclerosing panencephalitis (SSPE, years later). SSPE is a rare, but fatal degenerative CNS disease characterized by behavioral and intellectual deterioration and seizures that generally develop 7 to 10 years after measles infection.
- Immune "amnesia": Patients with measles are at higher risk for infectious diseases in the 2–4 years after measles infection, including for diseases they may have been previously immunized against or immune to. Maintain a lower threshold for testing/treating and refer to ID/immunology if there are concerns.

If patient received IVIG or IMIG

- No live-virus vaccines until 8 months after IVIG (recommendation based on receipt of 400 mg/kg dosing- timing may be variable if a different dose of IVIG was given, for example if patient was already on subcutaneous IG for another indication) or until 6 months after IMIG. Note, patients at high risk of exposure may receive live-virus vaccines sooner and then should be reimmunized after 11 months if they have an inadequate serological response.
- Risks of IVIG including: hemolytic anemia, aseptic meningitis.
- Most patients who receive IMIG have some discomfort and temporary mild swelling at the injection site.
- Note for patients weighing > 30 kg (66 lbs), IVIG is recommended over IMIG as they are unlikely to receive an effective dose via IMIG.

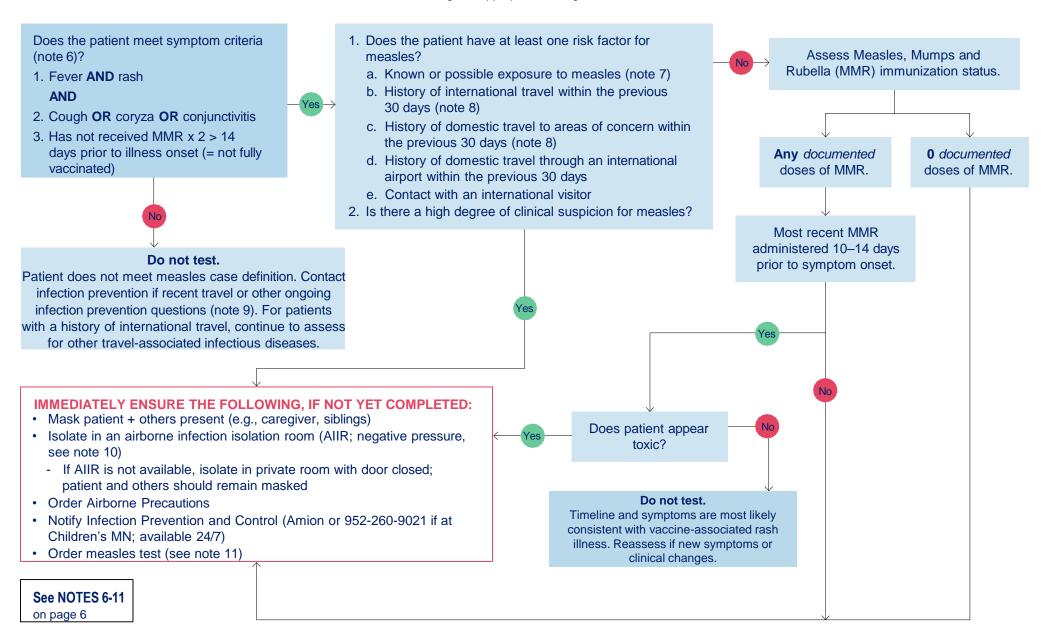
Post-exposure considerations (per CDC.gov)

- If a health care provider without evidence of immunity is exposed to measles, MMR vaccine should be given within 72 hours, or IG should be given within 6 days when available. Exclude healthcare personnel without evidence of immunity from duty from day 5 after first exposure to day 21 after last exposure, regardless of post-exposure vaccine.
- Infected people should be isolated for four days after they develop a rash; airborne precautions should be followed in healthcare settings.
- People without evidence of immunity who do not receive appropriate post-exposure prophylaxis within the appropriate timeframe should be excluded from affected institutions in the outbreak area until 21 days after the onset of rash in the last case of measles.

MEASLES TESTING ALGORITHM



Aim: To guide appropriate testing for measles.



MEASLES TESTING ALGORITHM



Aim: To guide appropriate testing for measles.

NOTE 6

- · Fever must be present at the same time as the rash, even if fever is subjective.
- Rash should start on the head or neck if the rash origin is known.
- Patients who have received 2 doses of MMR at least 10–14 days prior to symptom onset are very unlikely to have measles. Strongly consider alternate diagnoses.

NOTE 7

• Consider the patient to have a known exposure if the patient/family reports being notified by a healthcare facility or health department that they were exposed to a confirmed measles case. Consider the patient to have a possible exposure if the patient/family reports contact with a measles case.

NOTE 8

• Whether or not a patient meets a measles case definition, follow <u>Screening for Travel-Associated Infectious Diseases</u> for all patients with a history of international travel within the past 30 days.

NOTE 9

• Consult with Infection Prevention and Control (Amion or 952-260-9021 if at Children's MN; available 24/7) or compare patient's reported domestic travel to locations of current U.S. measles cases and outbreaks.

NOTE 10

- To determine locations of airborne infection isolation rooms (AIIRs; negative pressure), refer to <u>Airborne Infection Isolation (AII) and Protective Environment (PE) Patient</u> Rooms.
- If an AIIR is not immediately available, place the patient (and others with family, e.g., caregiver, siblings) in a regular room with masks on, place a portable HEPA filter unit (obtained from MESA) inside the room, and keep the door closed. Make arrangements to move the patient to an AIIR as soon as possible.

NOTE 11

• Refer to the "Measles Lab Testing Instructions" and order "Measles for Suspected Disease (Rubeola) to MDH" in Cerner OR "MEASLES PCR to MDH (UMSP)" in eCW.



REFERENCES

- Centers for Disease Control and Prevention. Measles Cases and Outbreaks: Measles Cases in 2019 2019. Available at: https://www.cdc.gov/measles/cases-outbreaks.html.
 Accessed November 13, 2019.
- American Academy of Pediatrics. Measles. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. Red Book: 2018 Report of the Committee on Infectious Diseases2018:537-550.
- World Health Organization. Measles vaccines: WHO position paper, April 2017–Recommendations. Vaccine. 2017;37:219-222.
- Hester GZ, Nickel AJ, Stinchfield PA, Spaulding AB. Demographics, Complications and Resource Utilization for Patients Hospitalized for Measles Across US Children's Hospitals. *Pediatric Infect Dis J.* 2019;38:977-978.
- Hussey GD, Klein M. A randomized, controlled trial of vitamin A in children with severe measles. N Engl J Med. 1990;323:160-164.
- D'Souza RM, D'Souza R. vitamin A for the treatment of children with measles a systematic review. Journal of tropical pediatrics. 2002;48:323-327.
- Barclay A, Foster A, Sommer A. vitamin A supplements and mortality related to measles: a randomised clinical trial. Br Med J 1987;294:294-296.
- Iannotti LL, Trehan I, Manary MJ. Review of the safety and efficacy of vitamin A supplementation in the treatment of children with severe acute malnutrition. J Nutr. 2013;12:125.
- Butler JC, Havens PL, Day SE, et al. Measles severity and serum retinol (vitamin A) concentration among children in the United States. Pediatrics. 1993;91:1176-1181.
- Hester GZ, Nickel A, LeBlanc J. Measles Hospitalizations at a United States Children's Hospital 2011-2017. Pediatr Infect Dis J. 2018.
- Mina MJ. Measles, immune suppression and vaccination: direct and indirect nonspecific vaccine benefits. J Infect. 2017;74:S10–7.
- Mina MJ, Metcalf CJE, De Swart RL, Osterhaus ADME, Grenfell BT. Long-term measles-induced immunomodulation increases overall childhood infectious disease mortality. Science (80-). 2015;348(6235):694–9.
- Mina MJ, Kula T, Leng Y, Li M, De Vries RD, Knip M, et al. Measles virus infection diminishes preexisting antibodies that offer protection from other pathogens. Science (80-). 2019;366(6465):599–606.
- https://radiopaedia.org/articles/measles
- UptoDate Measles
- UptoDate vitamin A
- National Foundation for Infectious Diseases Call to Action: vitamin A for the Management of Measles in the United States.
- www.nfid.org/measles
- https://www.cdc.gov/measles/hcp/index.html
- https://medicalguidelines.msf.org/viewport/CG/english/measles-16689967.html
- https://starnet.childrenshc.org/departments/infectioncontrol/pdf/measles-post-exposure-prophylaxis.pdf

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