Pennsylvania
Department of Health

Health Alert Network ADVISORY

Guidance for measles in pregnancy and congenital measles

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This transmission is an **Advisory** which provides important information for a specific incident or situation. May not require immediate action.

Intended Audience *(select below)*

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- ✓ **Health care providers:** Share with medical, pediatric, nursing, and laboratory staff.
- ✓ **Infection Preventionists**
- ✓ **EMS Councils, FQHCs & Local Health Jurisdictions**
- ✓ **Schools and Child Care Centers**
- ✓ **Accountable Care Organizations (ACOs)**
- ✓ **Long-Term Care Facilities:** Share with medical, infection control & nursing staff

Summary

- **Current situation:** Due to the ongoing measles outbreak, there is an increase in measles cases during pregnancy, along with rising concerns about congenital measles, which has been identified for the first time in decades. This advisory highlights and reinforces currently available guidance from medical professional societies on preventing and managing measles during pregnancy and after delivery. Guidance in this area continues to develop, and current recommendations incorporate professional input to support timely and safe care for pregnant women and their newborns.

- **Available guidance:** The American College of Obstetricians and Gynecologists (ACOG) published a practice advisory on the clinical management of pregnant individuals and those seeking to become pregnant during a measles outbreak.[1] The American Academy of Pediatrics (AAP) issued frequently asked questions addressing congenital measles.[2]
- **Safe and effective vaccine:** Measles in pregnancy can lead to serious adverse maternal and fetal outcomes. The measles, mumps, and rubella (MMR) vaccine is safe and highly effective. **Getting vaccinated BEFORE pregnancy is the best way to prevent measles and congenital measles.**
- **Prevention:** In non-outbreak settings, at least one dose of MMR vaccine should be offered to nonpregnant women of childbearing age without evidence of immunity. In outbreak settings, two doses should be offered separated by 28 days. MMR vaccine is a live vaccine. **The MMR vaccine should not be administered during pregnancy, and pregnancy should be avoided for 28 days after receiving MMR vaccine**[1,3-4].
- **Postexposure prophylaxis (PEP):** Non-immune pregnant women who are exposed to measles should receive intravenous immunoglobulin (IVIG) within 6 days of the initial exposure to reduce the risk of infection and lessen the severity if infection occurs.[4,6]
- **Congenital measles:** Neonates born after maternal measles symptom onset and through 14 days after maternal rash onset are at risk for symptomatic and transmissible measles infection. Evaluation and management should include measles testing, immunoglobulin (IG) administration, and empiric isolation.[2] All neonates born to women who had measles during pregnancy, regardless of gestational age at the time of measles infection, should be considered exposed to measles and may be at risk for congenital measles infection and its delayed complications, such as subacute sclerosing panencephalitis (SSPE).[2,5]
- **Breastfeeding:** MMR vaccination is safe for breastfeeding mothers. Breastfeeding does not interfere with immunity, and the measles vaccine is not transmitted through breast milk.[2,6]
- **Postpartum vaccination:** Postpartum mothers who are non-immune to measles should receive the MMR vaccine to protect themselves from measles infection and to reduce the risk of exposing their infants. Non-immune household members who live with or may be involved in the care of the infant should also receive the MMR vaccine. This can help to protect the infant during the first 6 months of life before they are eligible for the vaccine in an outbreak area.
- **Report immediately:** Providers caring for pregnant patients with suspected or confirmed measles, or evaluating newborns for possible congenital measles,

must immediately report suspected measles cases to your local public health department or to the Pennsylvania Department of Health (DOH) at 877-PA-HEALTH (877-724-3258). Providers are also encouraged to contact DOH for consultation.

Background

- Measles is a highly contagious, vaccine-preventable respiratory illness. The virus can remain airborne for up to two hours in an enclosed space and infects more than 90% of exposed non-immune individuals. It spreads mainly through the respiratory route and can also transmit transplacentally from a pregnant mother to the baby.[1-6] Approximately one-third of babies born to mothers with measles rash onset within 14 days of delivery will develop congenital measles.[5,7]
- Measles during pregnancy has been associated with an increased maternal risk of hospitalization, pneumonia, need for oxygen support or mechanical ventilation, and death.[1,3]
- Although evidence does not support an association between measles and teratogenesis, maternal infection during pregnancy is associated with an increased fetal risk of miscarriage, stillbirth, low birth weight, and preterm labor. Maternal infection, particularly in the 14 days prior to delivery, can lead to symptomatic, transmissible measles infection of the infant.[1-3]
- Clinical presentation of congenital measles (measles in the neonate) may vary widely, ranging from asymptomatic, to a mild illness in which the classic measles rash may or may not be present, to a rapidly fatal disease. Some neonates with congenital measles may develop symptoms at or after birth or may have delayed symptom presentation. Infants given IG at birth may remain asymptomatic despite measles virus detection.[2,5]
- All neonates born to mothers who had measles during pregnancy should be considered exposed to measles regardless of gestational age at the time of maternal measles onset. Although acute measles infection in utero may have occurred and resolved in some infants, they remain at risk for delayed complications, such as subacute sclerosing panencephalitis (SSPE). Families should be counseled to monitor for neurological signs or symptoms later in life, including seizures, regression in milestones, and academic difficulties in older children, which might indicate early signs of SSPE.[2,5,8]
- Another consequence of measles infection is immune amnesia, a form of immunosuppression of both cellular and humoral immunity months to years

following acute measles infection, which can increase susceptibility to various serious infections.[8-10]

Guidance for measles in pregnancy

A. General considerations for management of acute measles.

When managing patients who are exposed to measles or are suspected of having measles, the DOH recommends an approach including i) isolate, ii) identify, and iii) inform. The objectives are to minimize risk of transmission, provide a framework to identify and assess risk among persons exposed to or infected with measles, and remind providers to report measles to appropriate jurisdictions as soon as possible.

I) Isolate

- Patients who are exposed to measles or are suspected of having measles should be isolated immediately, ideally in a single-patient airborne infection isolation room (AIIR), if available or in a private room with a closed door until an AIIR is available.
- The patient should wear a surgical mask and avoid or limit time in the waiting area.
- Providers should expedite patient evaluation in an AIIR.

II) Identify

Measles risk assessment should include three components: 1) measles immunity, 2) exposure, and 3) clinical signs and symptoms.

- **Measles Immunity Assessment:** Health care providers should assess the measles immunity status of all patients, pregnant and nonpregnant. Presumptive evidence of immunity can be established in any of the following ways:[1,3-4,11]
    - Written documentation of having adequate doses of the MMR vaccine. For purposes of documenting immunity to determine if PEP is necessary, typically only one dose of vaccine is necessary; measles IG PEP is generally recommended for non-immune pregnant individuals, and for severely immunocompromised patients exposed to measles irrespective of prior vaccination status.[4,6] Separate from determining whether PEP might be necessary during outbreaks, as per ACOG recommendations and PA HAN 838, early accelerated and catch-up vaccination is encouraged for people who live in or plan to visit areas where there is sustained community transmission of measles.[12] Non-pregnant adults with no evidence of immunity should get two doses of MMR vaccine at least 28

days apart. Non-pregnant adults and teens who already received one dose of MMR vaccine should get a second dose at least 28 days after their first dose.[1] **Administration of MMR vaccine is contraindicated during pregnancy**.

- Laboratory evidence of immunity with measles IgG antibody tests. However, IgG antibody tests are not 100 percent sensitive and may fail to detect preexisting immunity[1,11]. While measles vaccine in the U.S. is given in a combined formulation as measles-mumps-rubella (MMR) vaccine, rubella immunity cannot be used as a proxy for measles immunity.[3,11]
- Laboratory confirmation of disease
- Birth before 1957

- **Exposure Assessment:** Rapid identification of exposed pregnant women is critical. IG PEP must be given within a 6-day window after initial exposure.
  - Measles patients are infectious from 4 days before rash onset to 4 days after rash onset. This means that an individual with measles can transmit measles to a susceptible individual in the highly infectious prodromal phase when infected patients do not yet have rash. Measles generally spreads from person to person by the respiratory route in shared airspace settings.[4]
  - Assess measles exposure risk by asking whether within the past 21 days the individual 1) had any contacts with a suspected or a known case of measles or 2) resided, visited, or traveled to a location where there is on-going measles community transmission. Refer to the DOH Measles Dashboard for the list of counties with ongoing community transmission.[12]
  - Measles exposure is defined as spending any amount of time without appropriate personal protective equipment in a shared airspace with an infectious person at the same time or in a shared airspace vacated by an infectious measles patient for up to 2 hours afterward.[4]
- **Clinical Assessment**: Health care providers should adhere to standard and airborne precautions for patients with suspected or confirmed measles. This includes respiratory protection that is at least as protective as a fit-tested, National Institute for Occupational Safety and Health (NIOSH)-certified disposable N95 respirator upon entry to the room or care area of a patient with known or suspected measles. N95 respirators should be worn regardless of

immunity status. Standard precautions should also be used based on the anticipated exposure (i.e., gloves, gown, eye protection, or face shield).

- The time from respiratory exposure to initial symptom onset averages 11–12 days, with a range of 7-14 days. The time from exposure to rash onset averages 14 days, with a range of 7–21 days.[4]
- Measles typically presents with a prodrome characterized by a fever of 38.3 °C (101 °F) or higher, and at least one of the three Cs: cough, coryza (runny nose), and conjunctivitis. Koplik spots, are often not present. The prodromal phase lasts 2–4 days or longer and is followed by a characteristic erythematous maculopapular rash that begins on the face and head and spreads caudally to the trunk and extremities.[4,6]

III) Inform

Providers should notify DOH at 877-PA-HEALTH (877-724-3258) or your local public health department immediately when suspecting measles, in pregnant and non-pregnant people.

B. Considerations for measles management based on risk assessment and stages of pregnancy

Primary prevention

- Providers should ensure that non-pregnant teenagers and adults previously vaccinated with one dose of MMR vaccine receive a second dose. Non-pregnant patients with no evidence of immunity should receive one dose of MMR vaccine immediately and follow with a second dose at least 28 days later.[1,3,11] Due to the theoretical risk to the fetus of the rubella component of the MMR vaccine, women should be counseled to avoid becoming pregnant for 28 days after receipt of the MMR vaccine.[1,3,11]
- MMR vaccine is contraindicated during pregnancy and should not be administered to women known to be pregnant or attempting to become pregnant.[1,3,11]
- Vitamin A supplementation does not prevent measles and is not a substitute for vaccination.[1,3,11] Pregnant women should not consume more than 10,000 IU of preformed vitamin A per day. Intake above this threshold before or during early pregnancy has been associated with a substantially increased risk of birth defects.[1,3]
- Postpartum mothers who do not have measles immunity should receive a dose of MMR vaccine prior to discharge home.[1,3]

- MMR vaccine is safe during breastfeeding and does not need to be delayed for lactation.[1-3]
- Non-immune household members who live with or may be involved in the care of the infant should also receive MMR vaccine. This can help to protect the infant during the first 6 months of life before they are eligible for the vaccine.

Postexposure consideration

Despite the challenge of recognizing measles exposure, particularly during the highly infectious prodrome period before rash onset, providers must stay vigilant, promptly assess potential exposure, and ensure susceptible individuals receive appropriate PEP within narrow time windows after exposure.[1,3-4,6]

Preconception period

- Non-immune nonpregnant women who are exposed should receive the MMR vaccine as PEP within 3 days after the initial exposure. Those vaccinated within this window do not need to be quarantined. Pregnancy should be avoided for 28 days after MMR vaccination.[1,3-4]
- Non-immune nonpregnant women who are exposed and do not receive the MMR vaccine as PEP should monitor symptoms and quarantine for 21 days.[4,6]
- Non-immune nonpregnant women who are exposed and are health care workers should be excluded from work from day 5 after initial exposure through day 21 after last exposure, regardless of receipt of PEP.[4,6]

Antepartum period

- Non-immune pregnant women who are exposed to measles should be offered IVIG as PEP within 6 days of the initial exposure. MMR vaccine should not be administered as PEP during pregnancy. Exposed pregnant women should monitor for symptoms and remain in quarantine for 21 days from the last exposure, or 28 days for those who receive IVIG.[4,6]
- Non-immune pregnant women who are exposed and are health care workers should be excluded from work from day 5 after initial exposure through day 21 after last exposure, if IVIG was not given, or through day 28 after last exposure, if IVIG was given as PEP.[4,6]
- Preterm labor should be considered a potential sign of measles infection in exposed non-immune pregnant women.[1,3,11]

Postpartum period

- If exposed, the postpartum mother who lacks evidence of measles immunity should receive MMR vaccine, as PEP within 72 hours of the initial exposure, and the neonate, if also exposed, should receive IG as PEP within 6 days of exposure.[1,4,6]

C. Measles diagnostic testing

Providers should offer measles testing for all patients suspected of having measles. Currently, testing is available at commercial laboratories, some academic medical centers, and at three Public Health Laboratories (PHL) in Pennsylvania, i.e., the PA Bureau of Laboratories (PA BOL), the Philadelphia Department of Public Health Laboratory, and the Allegheny County Health Department Public Health Laboratory.

For acute measles diagnosis, DOH recommends real-time reverse transcriptase polymerase chain reaction (RT-PCR) and serology tests (measles IgG and IgM). For expedited PCR testing through the PHL, providers should immediately contact DOH at 1-877-PA-Health (877-724-3258) or your local public health department for consultation and testing approval when suspecting measles. When a measles PCR test is positive in a recently vaccinated person, PA BOL can coordinate measles vaccine strain testing in a reference laboratory.

Specimens for PCR tests at PA BOL

Submit both a nasopharyngeal (NP) or oropharyngeal (OP) swab and a urine sample, following the PA BOL collection and submission guidance below.

- NP or OP swab in viral or universal transport media (VTM/UTM). ESwab in Liquid Amies transport medium is **not acceptable** for PA BOL measles PCR testing.
- Urine, at least 35 mL (minimum of 1 ml for newborns) in a sterile container
- Specimens for PCR testing must be maintained at ≤8 °C for up to 72 hours from collection. If held longer than 72 hours, they must be maintained at ≤0 °C. Failure to meet these requirements will result in immediate specimen rejection.
- **Ship all specimens on dry ice or sufficient cold packs in leak-proof container(s) to ensure acceptable temperature upon arrival**.

Serology testing for acute measles diagnosis including measles IgG and IgM should be sent to commercial laboratories.

D. Treatment of acute measles infection

Treatment of measles is supportive and includes rest, hydration, and antipyretics, as well as treatment of complications and secondary infections.

- There has been no established benefit of vitamin A as treatment for measles in pregnant adults. Furthermore, pregnant women should avoid taking high doses of vitamin A as it has been linked with severe birth defects.[1,3]
- When considering inpatient care, or when concerns of maternal and/or fetal complications exist, patients should be admitted to a hospital with an appropriate level of maternal and neonatal care and with appropriate infection control capacity.
- For cases in which a pregnant patient with suspected or confirmed measles is preparing for a cesarean delivery, clinicians should coordinate with the hospital to determine the right location for delivery as well as airflow considerations to limit transmission to other patients.[13]
- Measles is not an independent indication for delivery. Patients with measles who are at risk for preterm birth should be managed and offered antenatal steroids for fetal lung maturity similar to non-measles patients.[13]
- Pregnant women who recover from acute measles infection should have post-illness fetal monitoring.[13]

Guidance for congenital measles

Background

- Perinatal measles includes congenital infection acquired through transplacental or intrauterine exposure, as well as postnatal infection acquired through the respiratory route.[5]
- Neonates with clinical and/or laboratory evidence of measles infection within the first 10 days of life in the setting of intrauterine measles exposure are considered to have congenital measles infection.[2]
- The presentation of congenital measles infection is highly variable, ranging from asymptomatic, to the classic measles rash, to fulminant, multisystem disease and death. Common presentations include fever, rash, and jaundice. The classic maculopapular eruption may be atypical, delayed, or absent because of the infant's underdeveloped adaptive immune response, attenuation by passively acquired measles antibodies, or other reasons. Additional manifestations may include thrombocytopenia, pneumonia, and neurologic complications.[2]
- Congenital measles is distinct from neonatal measles. Neonatal measles is when exposure occurs postnatally through the respiratory route after birth.[5]

- In general, the time between respiratory exposure and measles rash onset (i.e., incubation period) ranges from 7–21 days.[4] For congenital measles, the incubation period ranges from 2–10 days, based on the interval between maternal rash onset and the baby's rash onset.[5]
- Neonates born at any gestational age should be considered at risk for symptomatic, transmissible congenital measles infection if birth occurs after maternal measles symptom onset through 14 days after maternal rash onset. This timeframe incorporates the reported maximum 10-day period between maternal and neonatal rash onset after in utero exposure plus an additional 4-day presumptive infectious period if congenital measles developed in utero and the neonate remained infectious at birth.[2]

E. Clinical management of neonates born to women with suspected or confirmed measles after maternal prodrome symptom onset through 14 days after maternal rash onset.[2]

- **Isolate**
  - Neonates born at any gestational age within 14 days of maternal rash onset should be delivered and managed in airborne isolation until infectiousness can be determined.
  - If a neonate is born asymptomatic during the maternal infectious period (from 4 days before through 4 days after rash onset), the neonate might be at risk for either manifesting congenitally acquired measles or being infected postnatally via respiratory droplets. There is limited data to inform separation of the mother and the neonate during the mother's infectious period after delivery. Determining maternal and neonatal separation requires a joint parent-provider decision that weighs the risk of respiratory exposure in addition to existing in utero exposure.
  - If the mother and neonate dyad is not separated during the mother's infectious period, they should be in an AIIR with 20 or more air changes per hour. The mother may consider using source control (e.g., NIOSH-approved disposable N95 respirator without an exhaust valve) to decrease potential risk of transmission to the neonate; however, data are not available to inform this practice.
  - Expressed breast milk can be given to the neonate regardless of separation.[2]

- **Identify**
  - Provider should perform a full evaluation of the neonate for signs and symptoms of congenital measles, and collect samples for measles testing, which include NP or OP swabs and urine for PCR and measles IgM.
- **Inform**
  - Providers should verify whether DOH or your local public health department is aware of the mother's diagnosis and delivery and notify DOH at 877-724-3258 or your local public health department immediately when managing a peripartum pregnant woman suspected of having measles.

- **At birth testing interpretation:**
  - **Negative** IgM or PCR in an **asymptomatic** neonate does not fully rule out congenital measles. Monitor these neonates for symptoms for 14 days after maternal rash onset and consider retesting.
    - If symptoms develop during the monitoring period, testing should be repeated.
    - If the neonates who tested negative at birth remain asymptomatic, consider repeat testing on day 10 of life to evaluate for evidence of in utero transmission. However, a negative repeat test might not exclude in utero transmission entirely. If admitted to a high-risk setting, additional caution may be warranted.
  - **Negative** IgM or PCR in a **symptomatic** neonate may also require repeat testing on at least day 10 of life, or as per the clinical judgment of the providers.
  - For neonates with a **positive** IgM or PCR test, consider the following:
    - Term and symptomatic with rash: isolation discontinuation may follow the conventional guidance, which is 4 days after rash onset. However, high-risk settings, such as the neonatal intensive care unit (NICU), may warrant a test-based approach, including two consecutive PCR tests, to determine when to discontinue isolation.
    - Term and asymptomatic: continue isolation and monitor symptoms during the 14 days after maternal rash onset.
    - Premature, symptomatic or asymptomatic: due to the possibility of prolonged infectiousness in premature neonates, a test-based approach including two consecutive PCR tests may be needed to determine discontinuation of isolation.

- **Considerations for IG and vitamin A for neonates born to women with suspected or confirmed measles[2]**
    - For neonates who are **asymptomatic** at birth,
        - IG PEP is indicated to prevent and attenuate congenital measles and also provide protection against postnatal transmission, if the mother is infectious at birth.
        - The effect of IG on the incubation period of measles infection may differ based on exposure route.
            - For postnatal respiratory-acquired measles, IG extends the incubation period from 21 to 28 days.
            - For in utero transmission, while data are limited, available literature suggests that rash onset occurs within a similar timeframe, regardless of the receipt of IG. Thus, symptom monitoring and empiric isolation for neonates who are only exposed in utero and receive IG as PEP should be considered on a case-by-case basis and should last at least up to 14 days after maternal rash onset.[2,14-17]
        - The role of vitamin A for asymptomatic neonates who are at risk for congenital measles is unclear.
    - For neonates who are **symptomatic** at birth,
        - Vitamin A should be given as part of supportive care for neonates with congenital measles with overt symptoms, unless there are contraindications to vitamin A. While vitamin A deficiency is rare in the United States, it has been associated with increased measles severity, mortality, and delayed recovery.[18]
        - While IG is generally recommended as PEP during the incubation period, its role during acute infection is unclear. However, given the immaturity of the neonatal immune system, IG administration may help reduce measles morbidity.

F. Clinical management of neonates born more than 14 days after maternal rash onset[2]

- Maternal measles can result in fetal exposure and pregnancy complications including miscarriage, stillbirth and preterm delivery. The clinical impact to the neonates if the pregnancy continues is uncertain. It is likely that active measles infection of the fetus had occurred and concluded by the time of the delivery.[1-2]
- If delivery occurs at or near term > 14 day after maternal rash, maternal measles IgG, developed in response to maternal measles, should have been

transferred to the neonate in utero, conferring immunologic control of measles replication.[2,19]

- Neonates born at 34+ weeks gestation with over 14 days after maternal rash onset are considered to **not** have risk for an acute symptomatic and transmissible measles infection after birth. Congenital measles infection may have occurred in utero, but a neonate would generally not be anticipated to be infectious at birth.[2,5]
- There is limited data to inform the management of neonates born more than 14 days after maternal rash onset. Measles testing, isolation, and IG administration should be considered on a case-by-case basis, based on maternal gestational age and immune status; neonatal factors, including clinical status and any identified congenital syndrome that may affect immunocompetence; and the care circumstances, including NICU admission or any high-risk settings.[2]

G. Post-acute and long-term sequelae in neonates born to mothers who had measles during pregnancy

- Most people with measles recover uneventfully. However, measles is more than just an acute illness: it is a systemic infection that can cause serious immunological and neurological sequelae.[2,8-10,18,20-21] All neonates born to mothers who had measles during pregnancy, regardless of gestational age at the time of maternal infection, should be considered exposed to measles. These neonates may be at risk for congenital measles and its delayed complications.[2,8-10]
- An important immunological sequela is immune amnesia, a form of immunosuppression of both cellular and humoral immunity that can persist for months to years after acute measles infection and increase susceptibility to severe secondary infections.[8-10]
- Measles-associated encephalitis is a rare but serious and potentially fatal complication. Primary measles encephalitis (PME) and acute postinfectious measles encephalomyelitis (APME) are two distinct conditions that typically develop days to weeks after the rash. Measles inclusion body encephalitis (MIBE) affects immunocompromised patients and occurs weeks to months after infection. Subacute sclerosing panencephalitis (SSPE) can occur months to years after apparent full recovery.[8,18,20-21]
- For infants and children with known history of congenital measles infection or known in utero exposure to measles, long-term clinical follow-up and vigilance for neurologic and immunologic complications are warranted. Parents should be carefully counseled, and providers should monitor for neurologic signs or

symptoms later in life, including seizures, regression in milestones, and academic difficulties in older children, which might indicate early signs of SSPE.[2,5,8]

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