

Measles and Patients with Inborn Errors of Immunity (IEI): Immunologic Basis of Susceptibility, Prevention, and Clinical Management

Measles infection provides a useful model for understanding host defense against viral pathogens. Protection requires coordinated humoral and cellular immunity.

Measles virus enters via the respiratory tract and initially infects immune cells through binding to activated lymphocytes and dendritic cells, followed by systemic dissemination. It is important to differentiate the immunologic mechanisms associated with the prevention of measles infection from those responsible for clearance of the infection once infection is established. Neutralizing IgG antibodies directed against measles surface glycoproteins acquired by previous infection, immunization, or passive immunity prevent viral attachment and entry into host cells and are the principal correlate of protection against infection. Once infection is established, CD8+ cytotoxic T lymphocytes recognize and eliminate infected cells (**Figure 1**).

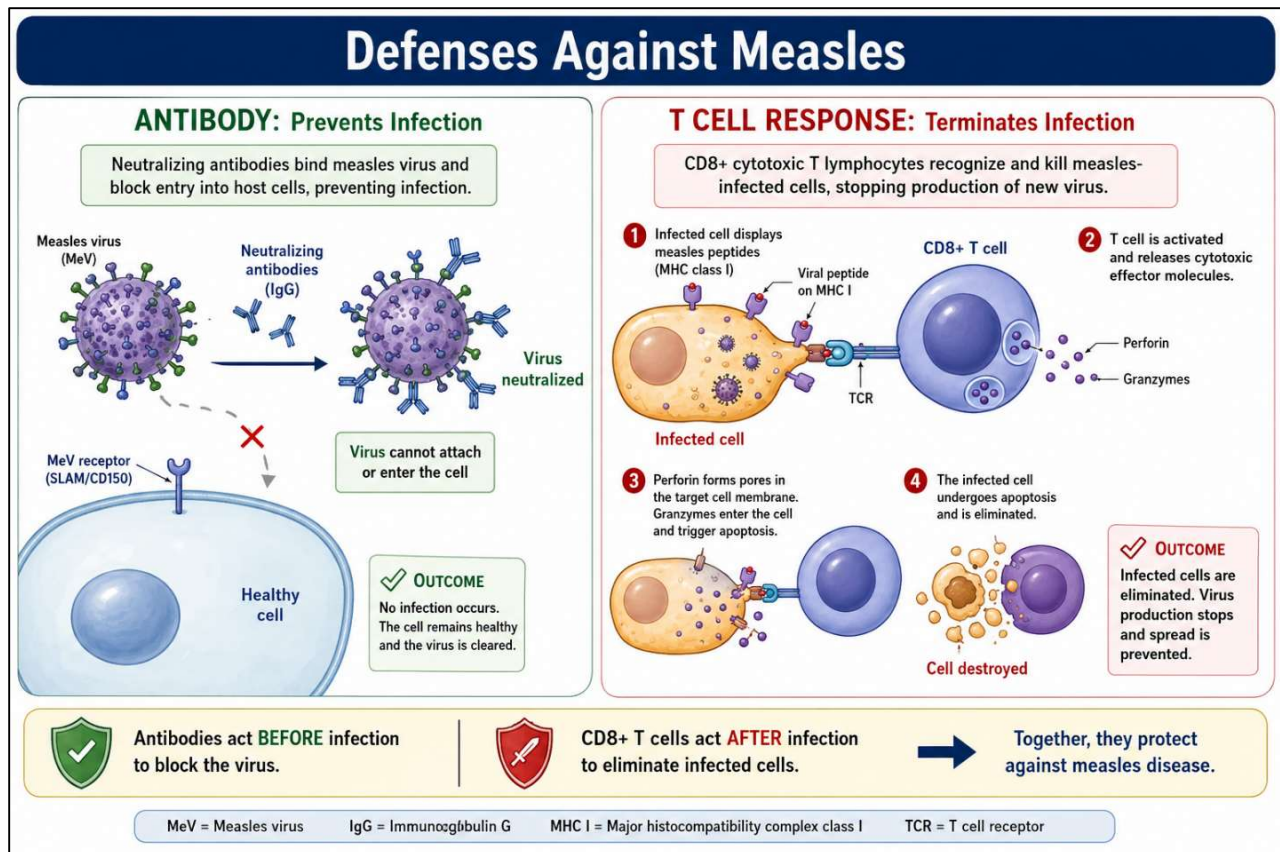


Figure 1. Schematic representation of antibody and cell-mediated immune (CMI) defense mechanisms against measles. Neutralizing antibodies prevent infection by blocking viral attachment and entry into host cells, whereas CD8+ cytotoxic T lymphocytes terminate established infection by recognizing and eliminating infected cells.

This framework helps explain why patients with significant T-cell defects are at highest risk for severe or persistent measles, and it provides a biologic basis for vaccine decision-making across

different IEI categories. This distinction is clinically important because susceptibility to measles infection is primarily determined by the presence of protective neutralizing antibody, whereas recovery from established infection depends largely on intact cellular immunity. *Figure created by the authors; no previously published material was used.*

Why is measles particularly dangerous for patients with IEI?

- Patients with IEI are at increased risk because of:
 - ✓ Impaired viral clearance
 - ✓ Prolonged viral shedding
 - ✓ Severe or atypical disease
- Higher rates of pneumonitis, encephalitis, and death
- Risk of persistent measles infection (including measles inclusion body encephalitis)
- Severe disease is highest with cellular immune defects (e.g., T-cell deficiencies, combined immunodeficiencies)

Which IEI patients are at greatest risk of severe measles?

Highest risk groups include:

- Severe combined immunodeficiency (SCID)
- Combined immunodeficiencies
- Significant T-cell lymphopenia
- DiGeorge syndrome with T-cell impairment
- Wiskott-Aldrich syndrome
- Hyper-IgM syndromes
- Patients receiving significant immunosuppression (post-transplant, biologics, or high-dose corticosteroids)
- Patients with antibody-only defects (e.g., XLA, CVID) may have a lower risk of disseminated disease if adequately treated with immunoglobulin replacement therapy, although risk is not completely eliminated.

Can patients with IEI receive the MMR vaccine?

While preventing measles through immunization is the priority, and public/patient messaging should recommend staying current with immunizations according to the AAP and AAFP schedules, the population of patients with IEI has special considerations.

Live attenuated MMR vaccine is contraindicated in:

- Severe T-cell defects
- SCID
- Significant combined immunodeficiencies
- Patients on substantial immunosuppression

May be considered in:

- Select mild antibody deficiencies
- Partial DiGeorge syndrome with adequate T-cell numbers and function
- Specific IEI where cellular immunity is intact

Although patients with isolated B-cell defects may safely receive live attenuated MMR due to intact cellular immunity, they may be unable to generate sufficient neutralizing antibody to achieve durable protective immunity. Immunoglobulin replacement remains the primary protective strategy in this population.

Vaccination decisions should be individualized and based on the degree of immune impairment, including one or more of the following parameters:

- Absolute CD3/CD4 counts
- Mitogen responses
- Clinical phenotype
- Published guidance (e.g., IDSA, CDC, ESID recommendations)

Does IVIG provide protection against measles?

Yes, standard IVIG contains measles-neutralizing antibodies. For patients receiving regular replacement IVIG (400–600 mg/kg every 3–4 weeks), circulating antibody levels are generally protective. However, timing of last infusion matters. No absolute protective titer is guaranteed. Patients receiving IVIG may not require additional post-exposure prophylaxis if adequately replaced.

What should be done if an IEI patient is exposed to measles?

Immediate steps:

- Confirm exposure details
- Determine date, duration, setting
- Confirm airborne exposure within 2 hours of an infected individual
- Assess immune status
- Confirm diagnosis
- Determine IVIG timing
- Assess vaccination history
- Administer immune globulin (IG) if indicated

Post-exposure prophylaxis (PEP):

- Administer intramuscular immune globulin (IMIG) within 6 days of exposure for susceptible individuals.
- IMIG: 0.5 mL/kg (max 15 mL); however, this may be impractical to obtain
- or administer in some cases.
- For severely immunocompromised patients, IVIG at a dose of 400 mg/kg is generally preferred for post-exposure prophylaxis.
- For patients already on replacement IVIG, additional dosing may not be necessary if infusion was recent. Consider trough level and time since last dose

Should IEI patients be isolated after exposure?

Yes, immunocompromised patients exposed to measles should:

- Avoid healthcare settings unless necessary
- Avoid school/daycare
- Monitor for symptoms for 21 days post-exposure
 - If IG was administered, monitoring may extend to 28 days.

How might measles present differently in IEI?

Classic measles:

- Fever
- Cough, coryza, conjunctivitis
- Koplik spots
- Maculopapular rash: The characteristic measles rash largely reflects the host T-cell-mediated immune response to infected tissues

In IEI, presentation may include:

- Absent or minimal rash because of the absence of T-cell-mediated immunity
- Severe pneumonitis
- Prolonged fever
- Encephalitis
- Persistent infection

How long is an infected IEI patient contagious?

Typical measles:

- 4 days before rash
- 4 days after rash

In IEI:

- Viral shedding may be prolonged
- Isolation may need to continue beyond standard duration

What about measles exposure in clinic settings?

Important precautions:

- Airborne isolation (negative pressure room)
- N95 for staff
- Avoid waiting room exposure
- Screen for fever/rash at check-in
- Consider telehealth for exposed IEI patients during monitoring period

What is measles inclusion body encephalitis (MIBE)?

MIBE is a rare but often fatal complication seen in immunocompromised patients. MIBE typically develops months after acute measles infection and presents as progressive neurologic deterioration. It results from persistent measles virus infection within the central nervous system and is associated with high mortality.

How should immunologists counsel families of IEI patients during outbreaks?

Key counseling points:

- Ensure household members are fully vaccinated
- Verify MMR status of siblings
- Avoid high-risk exposure settings during outbreaks
- Maintain timely IVIG infusions
- Have a clear action plan for exposure

Should household contacts of IEI patients receive MMR vaccine?

Yes, unless contraindicated. Egg allergy is not a contraindication for MMR vaccine.

MMR vaccination of household contacts is safe. Transmission of vaccine-strain measles virus from vaccinated household contacts has not been documented and should not be considered a contraindication to vaccination.

How long after IG administration can MMR vaccine be given?

Immune globulin interferes with live vaccine efficacy. After IMIG or IVIG, delay MMR vaccination for 3–11 months depending on dose.

For patients who cannot receive the MMR vaccine due to IEI, this may not be relevant, but it matters for household contacts.

What role should immunologists play during outbreaks?

Immunologists are uniquely positioned to:

- Guide IG prophylaxis
- Stratify risk in IEI patients
- Support primary care and hospital systems
- Develop institutional exposure algorithms
- Ensure immunoglobulin supply planning
- Enable contact tracing: notify local or state health department

Sources/citations for FAQ on measles and patients receiving immunoglobulin

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