



Measles in the Immunocompromised Host: Persistent Threats, Prevention Gaps, and Therapeutic Uncertainty

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No Disclosures



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The “Perfect” Storm?

CURRENT MEASLES EPIDEMIOLOGY



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Measles Cases Surge Worldwide

According to WHO and CDC estimates, there were 10.3 million measles cases in 2023, a 20% increase from 2022.

Countries experiencing large or disruptive outbreaks increased from 36 to 57.



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Minta AA. MMWR Morb Mortal Wkly Rep. 2024 Nov 14;73(45):1036-1042.

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Measles in 2025

■ Canada Measles Outbreak – October 2024 to April 2025

- As of April 3rd, Ontario has reported a total of 661 measles cases
 - Among all cases, 75.2% (497) were in infants, children, and adolescents, while 24.2% were in adults (160)
 - Among infants, children, and adolescents, 94.4% (469) were unimmunized, while among adults, 62.5% (160) were unimmunized
 - Fifty-two outbreak cases have required hospitalization; 50 were unimmunized

■ Europe

- The European Centre for Disease Prevention and Control describes 32,265 cases of measles between February 1st, 2024, and January 31st, 2025.
 - Rumania (27,568), Italy (1,097), Germany (637), Belgium (551) and Austria (542) reported the highest number of cases.
 - 85% of the cases (25,503) were unvaccinated
 - Rumania reported 18 deaths, and Ireland recorded 1

Public Health Ontario. Available from: <https://www.publichealthontario.ca/-/media/Documents/M/24/measles-ontario-epi-summary.pdf>

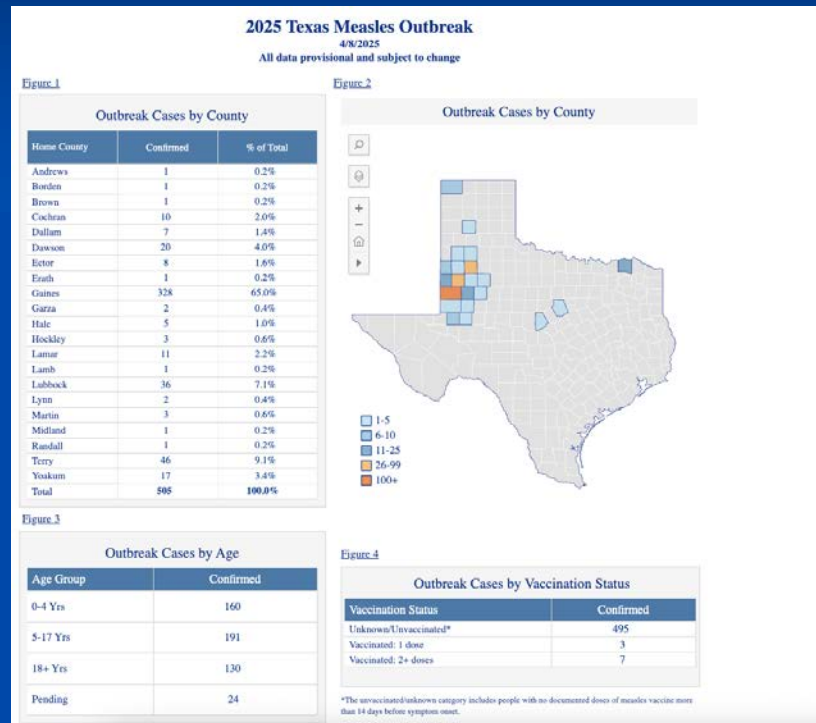
European Centre for Disease Prevention and Control (ECDC). Available from: <https://www.ecdc.europa.eu/en/news-events/measles-rise-again-europe-time-check-your-vaccination-status>



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Measles in Texas, United States



- The Texas Department of Health and Human Services reported 505 cases from late January 2025 to April 8th, 2025.
- Of the cases, 73% occurred in children and adolescents and 27% in adults.
- 98% of the cases have occurred in unvaccinated patients
- 11% (57) of the cases have required hospitalization
- Fifty-six of the patients have been hospitalized.
- There have been two fatalities; both were unvaccinated school-aged children.



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Texas Department of State Health Services. Measles Outbreak – April 8, 2025 Available from:
<https://dshs.texas.gov/news-alerts/measles-outbreak-2025>

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Measles - Transmission

- Measles is a highly contagious human pathogen, with an attack rate of 90% in measles nonimmune people.
- Transmission occurs via airborne routes when an infected person releases infectious droplets and aerosols by coughing, sneezing, or breathing.



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Hubschen JM. Lancet. 2022 Feb 12;399(10325):678-690.
Simpson RE. Lancet. 1952 Sep 20;2(6734):549-54.

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The Prevalence of Immunosuppression is Increasing

2013 NHIS

Immunosuppression Prevalence

2021 NHIS

Immunosuppression Prevalence

2.7% → 6.6%



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Martinson ML. JAMA. 2024 Mar 12;331(10):880-882.

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Measles – Immunocompromised Host

- Immunocompromised hosts are at risk for severe measles, and a higher risk of complications and mortality may be expected.
- Since the development of a rash is associated with the onset of immunity, immunocompromised hosts may present without a rash or with an atypical one.
- Giant cell interstitial pneumonitis and inclusion body encephalitis may occur without a rash.



Measles – Secondary Infections

- Several immune alterations have been associated with measles virus infection, including T-cell lymphopenia with depletion of T-dependent areas of lymph nodes and spleen, diminished T-cell proliferation and reduced antibody production.
- Secondary infections include bacteremia, bacterial and viral pneumonia, and otitis media.
- Tuberculosis reactivation in the setting of recent measles infection has also been described.
- Measles associated immune defects may account for increased mortality up to three years following infection.





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Can We Do Better?

MEASLES DIAGNOSTICS



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Measles - Diagnosis

- Testing patients most likely to have measles is essential to maximize diagnostic performance.
- Testing for all suspected measles cases includes serologic (IgM & IgG) testing and RT-PCR to optimize sensitivity and specificity.

Centers for Disease Control and Prevention. Chapter 7: Measles. In: Manual for the Surveillance of Vaccine-Preventable Diseases [Internet]. 6th ed. Atlanta (GA): Centers for Disease Control and Prevention; 2013 [cited 2025 Apr 9]. Available from: <https://www.cdc.gov/surv-manual/php/table-of-contents/chapter-7-measles.html>.



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Measles – Serologic Testing

■ IgM – Acute Illness

- Appear within 1-4 days of rash onset and peak within the first week
- It is most sensitive ≥ 3 days after rash onset
- Can be detected for 6-8 weeks following acute measles infection
- False positives will be common in the setting of low pre-test probability
- Interpret with caution in patients who recently received IVIg

■ IgG - Tests for pre-existing immunity

- Detection of IgG at the time of rash onset, or after exposure and prior to rash onset represents prior immunity
- Interpret with caution in patients who recently received IVIg



Measles – RT-PCR

- Measles RNA detected (RT-PCR)
 - Efforts should be made to obtain a throat (OP) or nasopharyngeal (NP) swab from suspected cases
 - Sensitivity is highest within the first three days of rash onset, but virus can be detected up to ten days after rash onset
 - Urine samples may also contain virus, and when feasible, should be tested
 - Commercial assays cannot distinguish between vaccine-derived virus or wild-type virus
- Measles Vaccine (MeVA) Assay
 - Available at the CDC to determine if detected measles virus is vaccine-derived or wild-type virus



MEASLES PREVENTION



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Measles – Presumptive Evidence of Immunity

- The US Centers for Disease Control and Prevention defines presumptive evidence of immunity, to measles, in any of the following ways:
 - Laboratory confirmation of disease
 - Birth before 1957
 - Written documentation of adequate vaccination with MMR. Two doses at least 4 weeks apart are required during an outbreak
 - Laboratory evidence of immunity (positive Measles IgG)
- Patients not meeting the above criteria are considered nonimmune and should be vaccinated unless contraindicated



Vaccination as Measles Post-Exposure Prophylaxis

- A study conducted in children during a measles outbreak in New York City in 2013 found that MMR was effective as post-exposure prophylaxis at 83.4% (95% confidence interval, 34.4% to 95.8%) when administered within 72 hours of exposure
- A systematic review reported that the effectiveness of MMR as post-exposure prophylaxis ranged from 83.4% to 100%.
 - Six studies were included. MMR PEP was administered within 72 hours of exposure
 - Adults were under-represented in the studies, and comorbid illness not described



Cochrane Review - Immunoglobulin as Measles Post-Exposure Prophylaxis

■ Methods

- A Cochrane review assessed the effectiveness of intramuscular or intravenous immunoglobulin for preventing measles in exposed susceptible individuals.
- The study included one RCT, two quasi-RCTs, and 10 cohort studies, totaling 3925 participants.
 - Only one study included adults among the participants, although four studies did not report the age of the participants, and five studies didn't provide a clear age range.
 - The proportions of participants at high risk of measles complications were poorly reported.

■ Results

- When given within seven days of exposure, immunoglobulins effectively prevented measles, compared to no treatment, with a risk ratio of 0.17 (95% CI 0.08 to 0.36).
- Immunoglobulin effectively prevented death due to measles compared to no treatment, with a risk ratio of 0.24 (95% CI 0.13 to 0.44)



Effectiveness of Immunoglobulin as Measles Post-Exposure Prophylaxis – New York City, 2013

■ Methods

- Retrospective cohort study of patients of children (< 19 years of age), without presumptive evidence of measles immunity exposed to measles as defined by the CDC during a New York City outbreak in 2013 were included.

■ Results

- A total of 3409 contacts were identified, 274 met inclusion criteria for analysis of immunoglobulin post-exposure prophylaxis
- Of the contacts included 77 received immunoglobulin as recommended by the CDC.
- No contacts who received immunoglobulin post-exposure prophylaxis developed measles
- the effectiveness of immunoglobulin post-exposure prophylaxis was 100% (approximated 95% CI 56.2%,99.8%)



Caveats of Current PEP Studies for ICH

- Vaccination as PEP
- Immunoglobulin as PEP
 - Studies have included few adults with the comorbidities
 - Feasibility of large-scale implementation of immunoglobulin infusion
 - Unclear who would benefit the most from the infusions
 - The patient remains susceptible after the effect of IG is gone



Remdesivir for Measles Post-Exposure Prophylaxis in Rhesus Macaques

■ Introduction

- Remdesivir is an IV nucleoside analog that inhibits the RNA-dependent polymerase of measles

■ Methods

- Nine 2- to 3-year-old Indian-origin, measles seronegative, rhesus macaques were inoculated intratracheally with wild-type measles virus (D=0)
- Six received intravenous remdesivir 100mg/kg loading dose followed by 5m/kg starting on D=3 for 12 days. Three received matching placebo.
- Two study veterinarians blinded to the study group monitored the macaques and scored them for clinical symptoms with a 10-parameter scale. Macaques also had absolute lymphocyte counts, and RNA and viral cultures were performed in PBMCs.

■ Results

- The 10-parameter scale did not differ in the treatment vs. control group.
- Remdesivir lowered viral RNA levels in PBMCs, but RNA rebounded at the end of therapy, and the virus was consistently isolated.
- There was no difference in the nadir absolute lymphocyte count between groups.



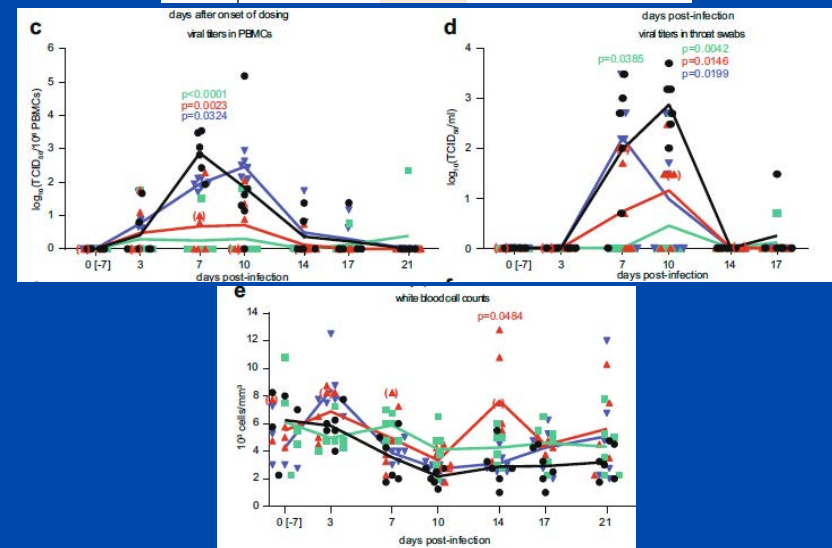
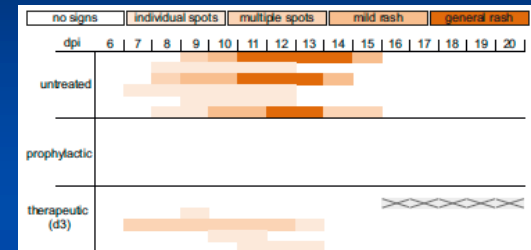
ERDRP-0519 for Measles Prophylaxis and Post-Exposure Prophylaxis in Squirrel Monkeys

■ Introduction

- ERDRP-0519, an oral small molecule, fully inhibits phosphodiester bond formation by the morbillivirus RNA-dependent RNA-polymerase.

■ Methods

- Twelve squirrel monkeys were inoculated with the Measles Virus FrankfurtMain.DEU/17.11 intranasally
- Six started ERDRP-0519 50mg/kg BID 12 hours before inoculation and continued for 14 days, and six remained untreated.
- Six started ERDRP-0519 50mg/kg BID D+3 inoculation and continued for 14 days, and six remained untreated.



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Cox RM. PLoS Pathog. 2021 Feb 23;17(2):e1009371.
Wittwer K. Nat Commun. 2021 Sep 2;12(1):5233.

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Do We Have the Right Tools?

MEASLES TREATMENT



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Measles Treatment

- The treatment of measles is supportive; there is no specific antiviral therapy approved for treatment of measles.
- Vitamin A deficiency contributes to delayed recovery and to risk of complications. There is a role for Vitamin A only in selected scenarios. It is recommended for children with severe measles, and children with measles in resource-limited settings.
- There is insufficient evidence to recommend the use of ribavirin for the treatment of measles.



Remdesivir for Measles Treatment in Rhesus Macaques

■ Methods

- Six 2- to 3-year-old Indian-origin, measles seronegative, rhesus macaques were inoculated intratracheally with wild-type measles virus (D=0)
- Three received intravenous remdesivir 100mg/kg loading dose followed by 5m/kg starting on D=12 (onset of rash) for 12 days. Three received matching placebo.
- Two study veterinarians blinded to the study group monitored the macaques and scored them for clinical symptoms with a 10-parameter scale. Macaques also had absolute lymphocyte counts, and RNA and viral cultures were performed in PBMCs.

■ Results

- The 10-parameter scale was higher in the treatment group compared to placebo.
- Remdesivir had little impact on viral RNA levels
- Although the nadir ALC was similar, at the end of the follow-up, the ALC was higher in the treatment group.



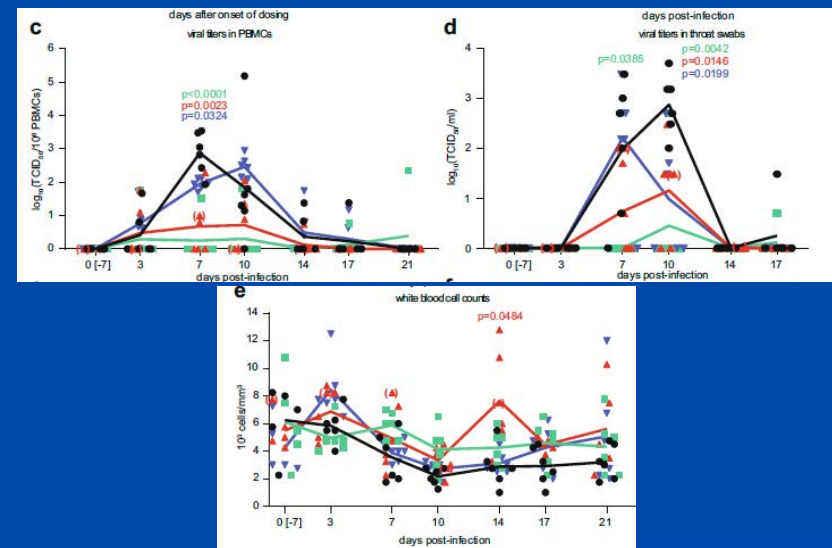
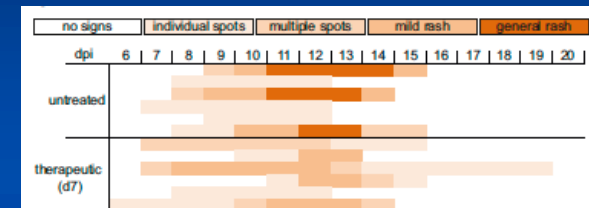
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Conclusions

- There is an ongoing threat of measles worldwide.
- The proportion of immunocompromised hosts is increasing.
- A high morbidity and mortality is expected for ICH with measles.
- We need diagnostic tools to diagnose ICH patients during the prodrome phase.
- There is no safety to support using measles vaccination in adult immunocompromised hosts.
- It is unclear which subgroups of the ICH population will benefit the most from PEP with IG.
- We do not have effective approved therapies for the treatment of measles.



