

The Next Outbreak Looms on the Horizon: Measles and Potential Impacts on Transplant Recipients

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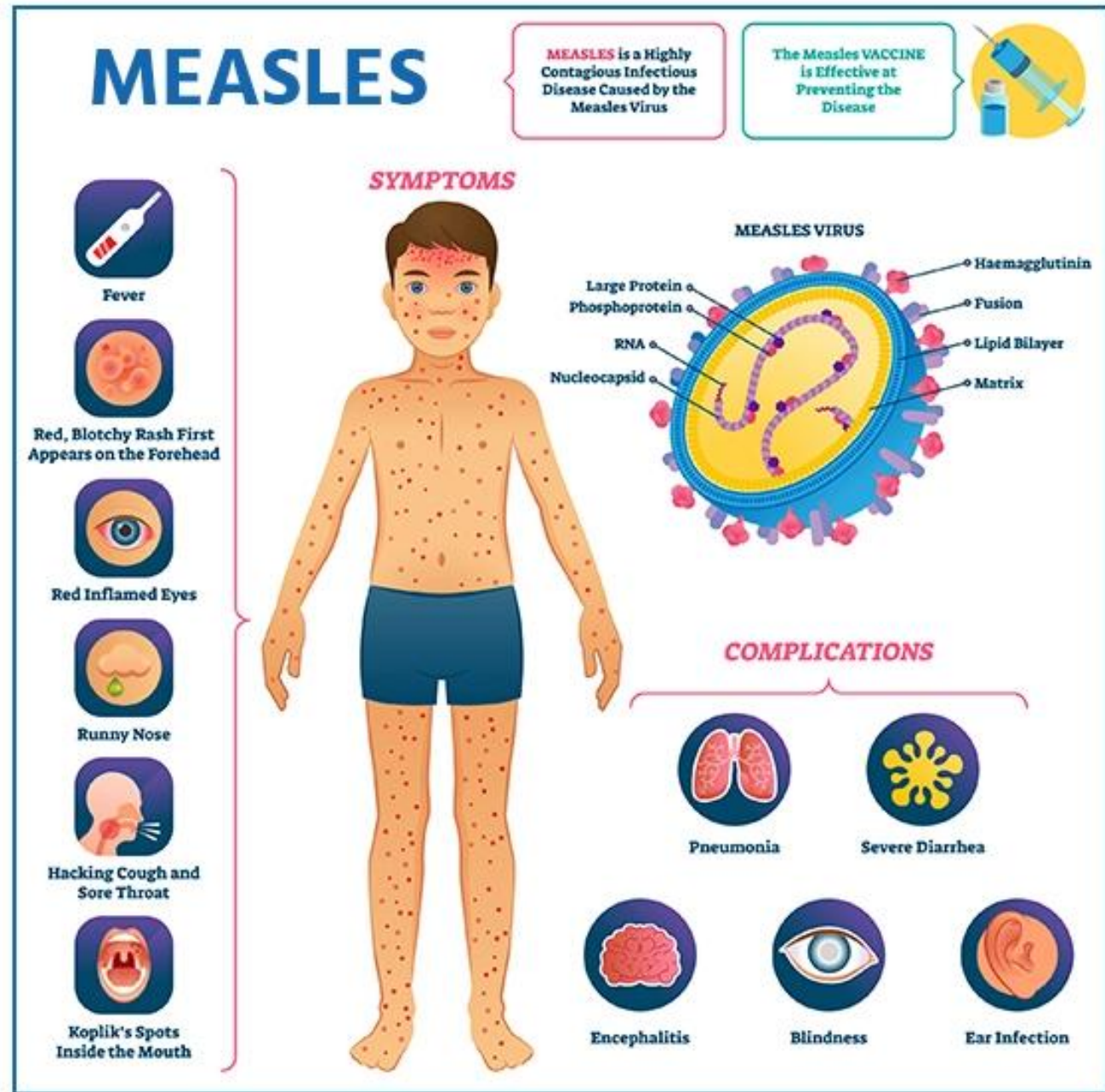
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- **Camille N. Kotton, MD served on the Advisory Committee on Immunization Practice at the US Centers for Disease Control and currently serves as a consultant**
- **She serves as a consultant for Biotest and Kamada**

What is measles?

- transmitted via airborne spread or respiratory droplets
- among the **most contagious of pathogens** with infection occurring in up to 90% of nonimmune close contacts
- a **single case of infection is estimated to cause 12–18 secondary cases** in susceptible individuals
- may be **even more contagious in susceptible immunocompromised populations**



THREAT ASSESSMENT BRIEF

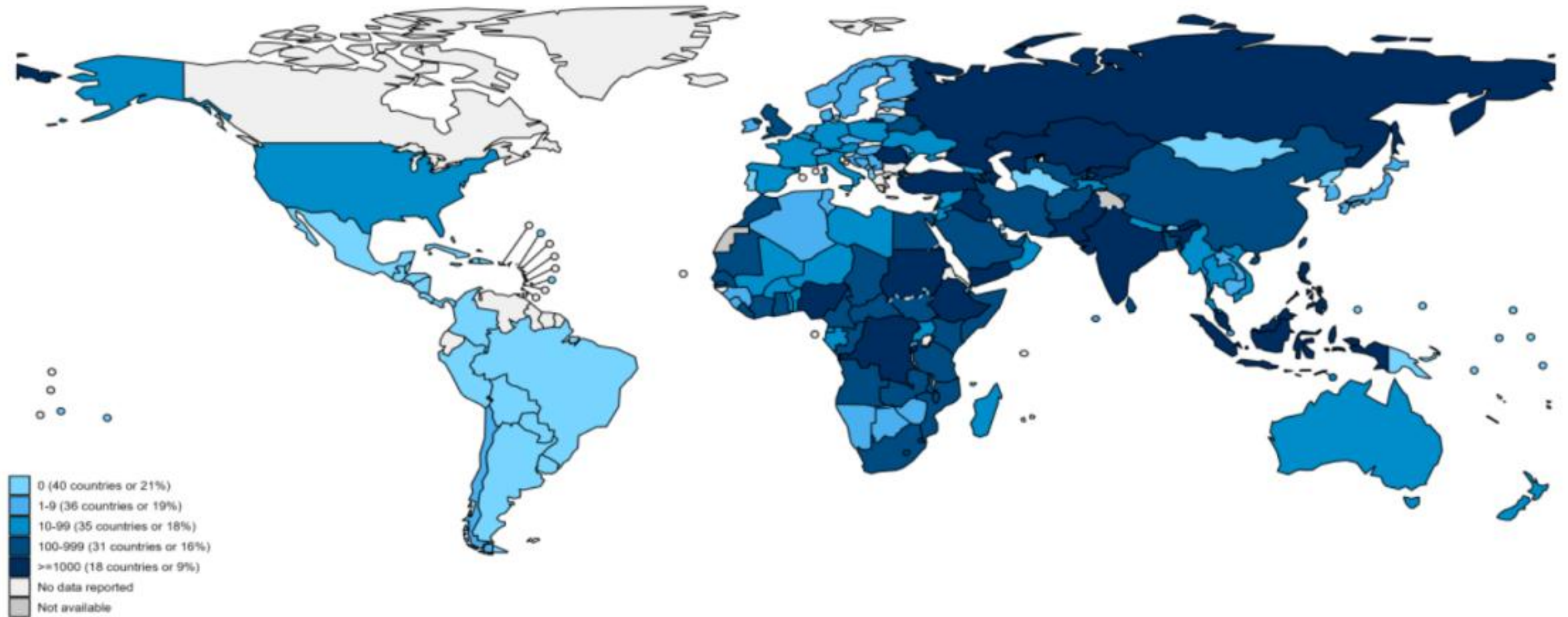
Measles on the rise in the EU/EEA: considerations for public health response

16 February 2024

Summary

In 2023, significant increases in the number of measles cases and outbreaks were observed globally, including in 40 of the 53 countries of the European region, and in at least ten EU/EEA countries. Measles cases are expected to continue increasing in the EU/EEA in the coming months due to sub-optimal vaccination coverage for measles containing vaccines (MCV) in a number of EU/EEA countries, the high probability of importation from areas experiencing high circulation and the fact that the coming months represent the seasonal peak of the virus.

Geographic distribution of the number of reported cases of measles, July – December 2023

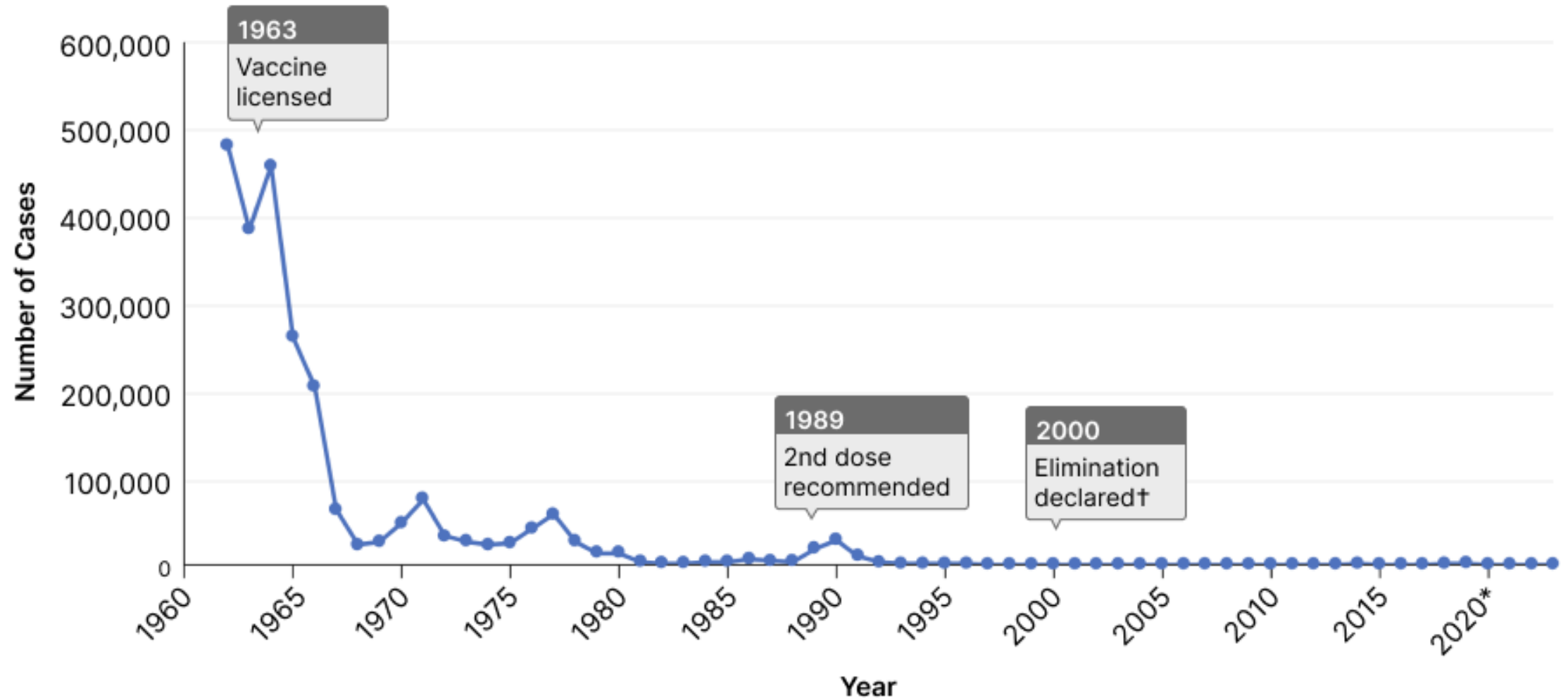


Map production: World Health Organization, 2024. All rights reserved
Data source: IVB Database

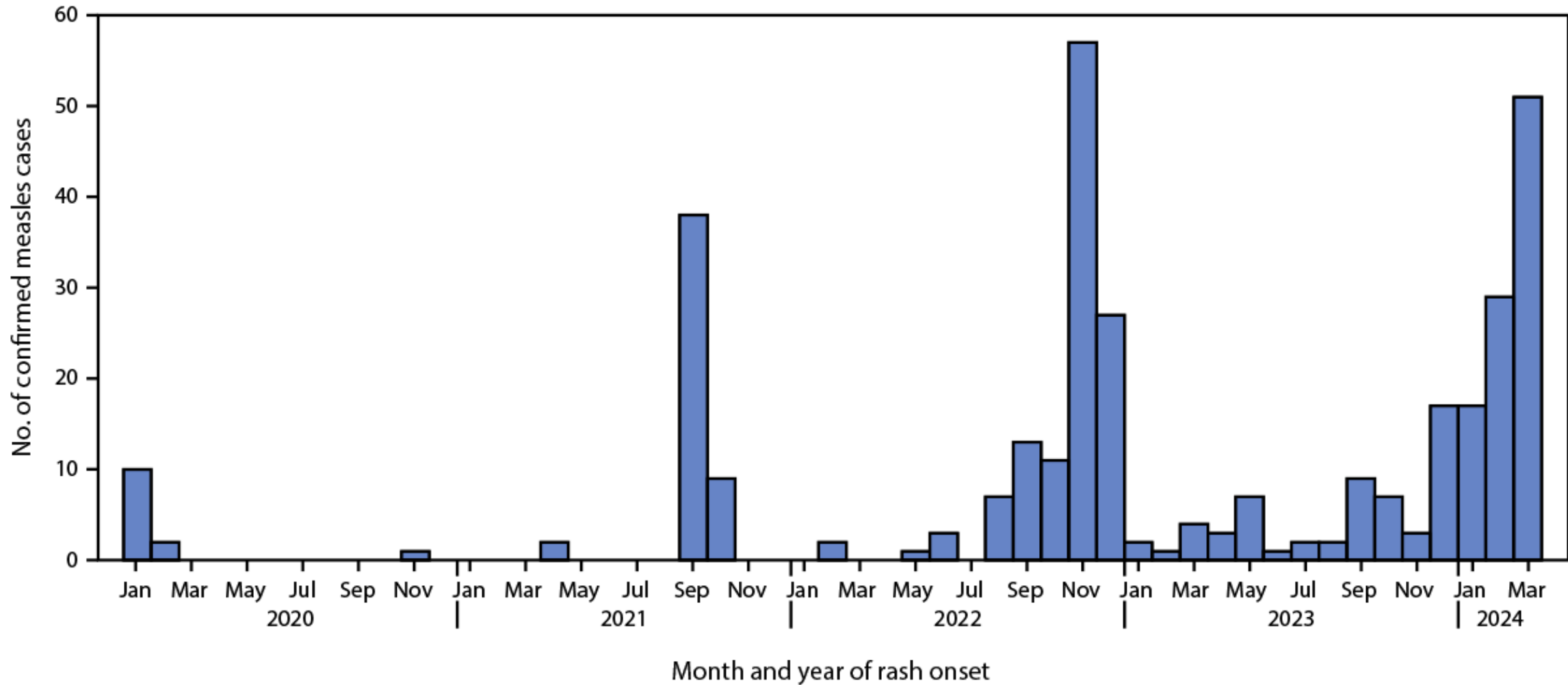
Disclaimer: The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

0 875 1750 3500 Kilometers

Reported Measles Cases in the United States from 1962 – 2023*



Confirmed measles cases (N = 338) — United States, January 1, 2020–March 28, 2024



About 1 in 5

people in the US who get measles
will be hospitalized



National
Foundation for
Infectious
Diseases

www.nfid.org/measles

Up to **9** in **10** people who lack immunity to measles and are close to an infected person will become infected



1-3 out of **1,000** people with **measles**
will die, even with the best care

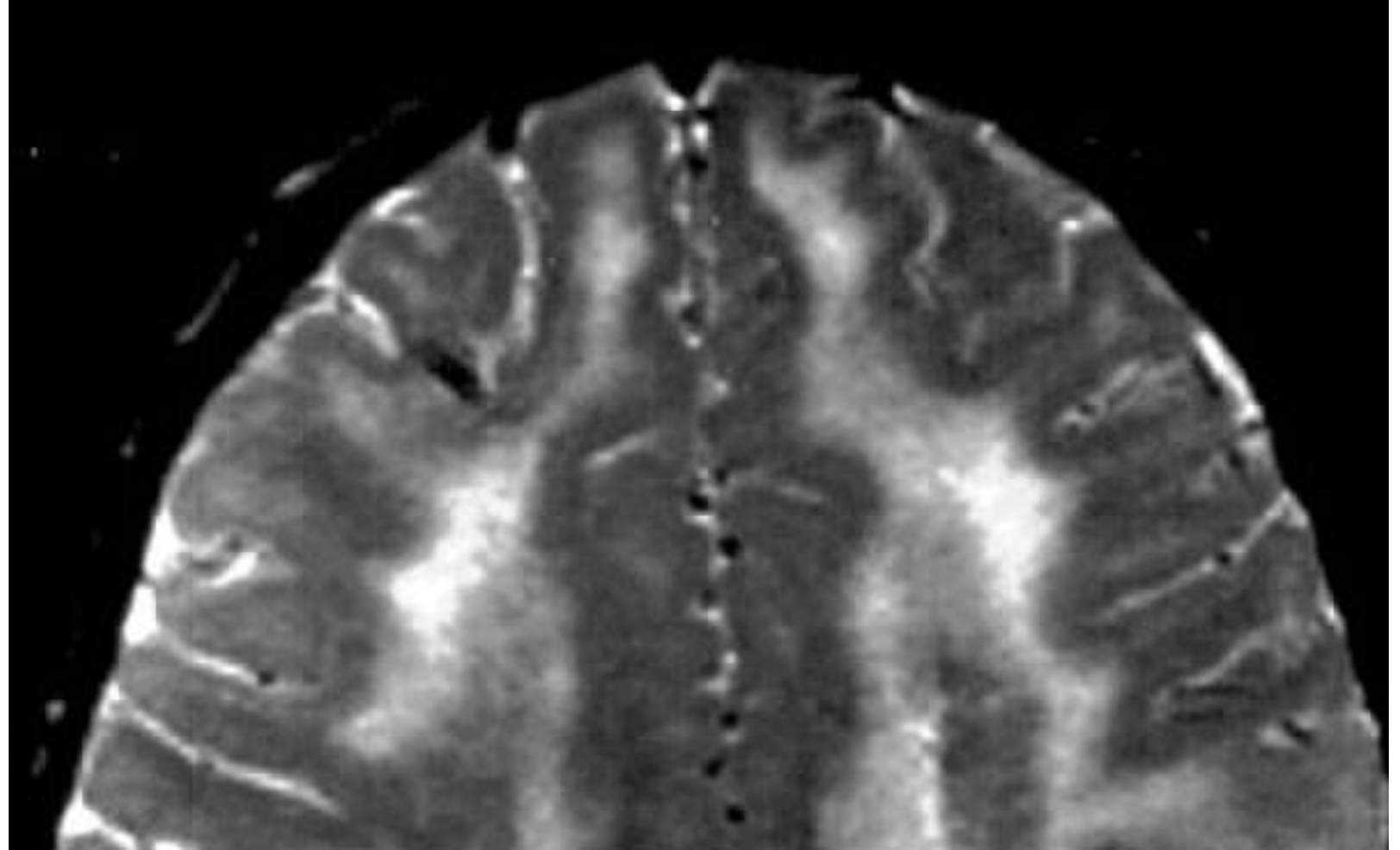


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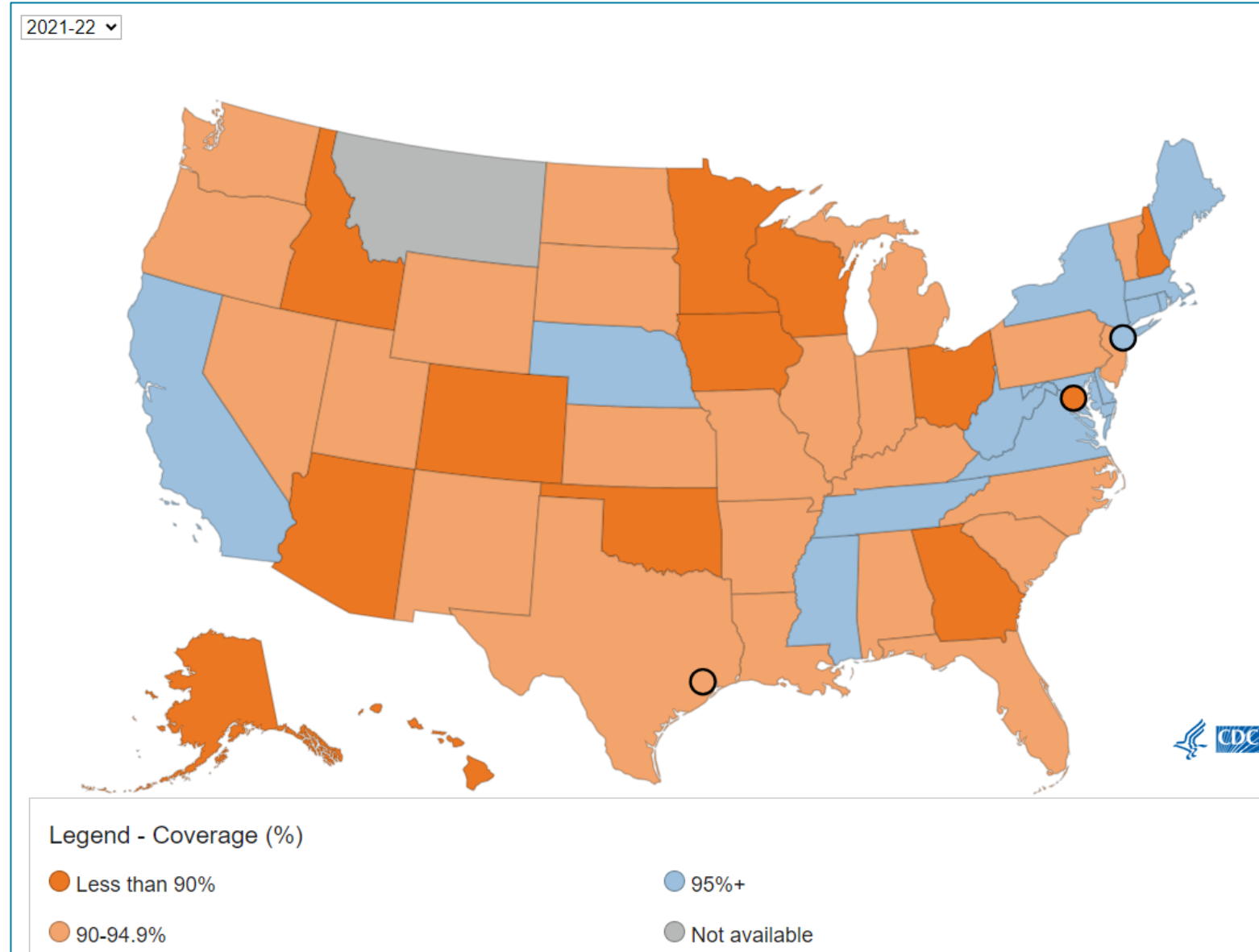
Complications from Measles

- Acute disseminated encephalomyelitis (ADEM):** demyelinating disease of the central nervous system that develops in 1:1000 cases
- Measles inclusion body encephalitis** (typically in immunocompromised individuals 6–12 months after infection)
- Subacute sclerosing panencephalitis**, a fatal progressive neurodegenerative disease years later in roughly 1:10,000



MMR Vaccine Coverage for Kindergarteners by School Year

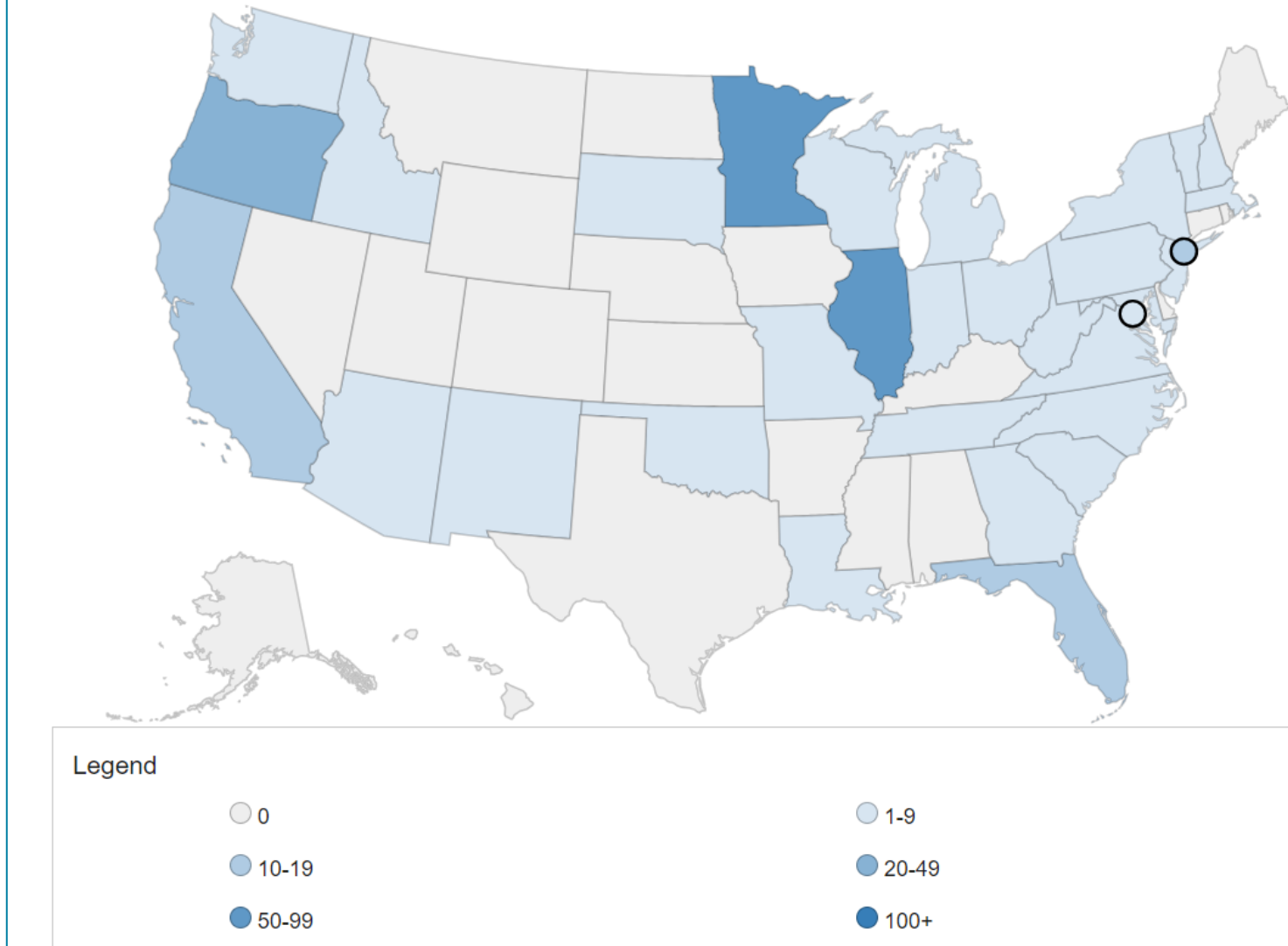
vaccination of $\geq 95\%$ of the population is needed to obtain enough community immunity to prevent measles outbreaks



<https://www.cdc.gov/measles/data-research/index.html>

Measles Cases in 2024

as of September 26, 2024



<https://www.cdc.gov/measles/data-research/index.html>

The majority of current transplant recipients in the United States were born after 1957 and before the late 1970s, the cohort at highest risk for poor protection from prior vaccine per the CDC

- less likely to have been infected in childhood and may have only had a single dose of vaccine, which provides inadequate protection and led to outbreaks of disease

In a series from Houston, 20% of transplant candidates were measles seronegative before transplant¹

In a series of 672 transplant candidates from Salt Lake City, 13% were measles seronegative²

IN COMBINATION WITH IMMUNOSUPPRESSION, TRANSPLANT RECIPIENTS ARE EXCEPTIONALLY VULNERABLE TO MEASLES

1. Javaid H, Prasad P, De Golovine A, et al. Seroprevalence of measles, mumps, rubella, and varicella-zoster virus and seroresponse to the vaccinations in adult solid organ transplant candidates. *Transplantation*. 2023;107:2279–2284.

2. Schneider S, Carlson A, Sirandas B, et al. Serologic evaluation of vaccine preventable infections and vaccination rates in kidney transplant candidates. *Transpl Infect Dis*. 2022;24:e13973.



Transplantation 2024

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Ayman Al Jurdi, MD¹ and Camille N. Kotton, MD²

TABLE 1. Prevention of measles in transplant candidates and recipients through vaccination and immunoglobulin			
Strategy	Dosing	Advantages	Comments
MMR vaccination	Two doses given at least 4 wk apart	Most effective prevention strategy	Recommended only before transplantation in adults due to risk of live vaccine-associated disease(s) May be safe in pediatric recipients on lower immunosuppression A minimum of 4 wk should separate the last vaccine dose from immunosuppression for transplantation
Intravenous immunoglobulin postexposure prophylaxis	One dose of 400 mg/kg given within 6 d of exposure	Rapid protection, safe for transplant recipients (and candidates) on immunosuppression who cannot get MMR vaccine	Lack of high-quality data demonstrating effectiveness in transplant recipients Different formulations and batches may have different amounts of anti-measles antibodies Expensive, cumbersome, and has potential side effects Protects short term but not longer term
Intramuscular immunoglobulin postexposure prophylaxis	One dose of 0.5 mL/kg (maximum dose = 15 mL)		

Based on the Centers for Disease Control and Prevention. Recommendations. Available at <https://www.cdc.gov/mmwr/preview/mmwrhtml/rr6204a1.htm>. Accessed March 3, 2024 and the Infectious Disease Society of America. Accessed March 3, 2024; Rubin LG, Levin MJ, Ljungman P, et al: 2013 IDSA clinical practice guideline for vaccination of the immunocompromised host. *Clin Infect Dis*. 2014;58:e44–e100.

A 57 year old organ transplant recipient in New York city comes to transplant clinic for a routine visit 3 months after emergent liver transplant

Was measles seropositive at the time of transplant (after many transfusions and fresh frozen plasma)

Astute infectious disease specialist noted that prior measles serology in outside record was negative

He reports not feeling well for a few days, and on exam, has a low grade fever and rash

He was in the crowded transplant clinic waiting room for a hour before the visit

All transplant recipients in the waiting room (and afterwards) should get IVIG 400mg/kg within 6 days

Why is it so important to prevent measles?

Currently, there is no effective treatment for measles beyond vitamin A and supportive care

Remdesivir*

very limited data from *in vitro* measles virus dissemination assays suggest it may have a role in postexposure prophylaxis or treatment

post-exposure prophylaxis in rhesus macaques: safe and decreased measles virus replication but did not improve clinical outcomes or lymphopenia

further study needed in animal models and humans

Ribavirin**

results depend on the timing and dosage of the treatment

in US, only under a FDA investigational new drug application (IND)

*Peart Akindele, N.A., Katamoni, L.D., Brockhurst, J. et al. Effect of remdesivir post-exposure prophylaxis and treatment on pathogenesis of measles in rhesus macaques. Sci Rep 13, 6463 (2023). <https://doi.org/10.1038/s41598-023-33572-7>

**Liatsos G. D. (2021). Controversies' clarification regarding ribavirin efficacy in measles and coronaviruses: Comprehensive therapeutic approach strictly tailored to COVID-19 disease stages. World journal of clinical cases, 9(19), 5135–5178. <https://doi.org/10.12998/wjcc.v9.i19.5135>

Clinical disease: may be atypical presentation in transplant recipients

Laboratory testing can confirm the presence of measles infection via:

real-time PCR (RT-PCR)** (best in immunocompromised)

isolation of measles virus in cell culture

detection of measles IgM

detection of a 4x rise in measles IgG (enzyme immunoassay or hemagglutinin inhibition)

Specimens are taken from the upper respiratory tract, blood serum, nasopharynx, or urine.

In certain cases, alternative specimens can be used for testing, including bronchoalveolar lavage, cerebral spinal fluid, or tissue biopsies.

Combination testing, including serology and RT-PCR from multiple clinical sites for sampling, improves diagnostic sensitivity.

- Highlight the importance of this topic as it can be challenging to find information about protecting exposed immunocompromised patients
- Develop/provide information regarding various immunoglobulin products for post-exposure prophylaxis (or pre-exposure in high-risk settings, e.g. travel to an endemic region): e.g. dosing, likelihood of protection, duration of protection based on anticipated PK/PD
- Enhance MMR vaccination when not on immunosuppressive agents
- Consider developing clinical trials (or enhancing access) with antiviral agents in immunocompromised patients with measles
- Optimize and increase access to acute diagnostics

A wide-angle photograph of a city skyline, likely Boston, featuring a prominent blue glass skyscraper and other modern buildings. In the foreground, there is a body of water (the harbor) with a small boat, and a line of green trees separates the water from the city.

Discussion welcomed

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