Public Health Perspective: Federal Level

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Centers for Disease Control and Prevention
Viral Vaccine Preventable Diseases Branch
Viral Classification Meeting
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Disclaimer and Introduction

The findings and conclusions in this presentation are those of the author and not necessarily those of the Centers for Disease Control and Prevention.
Measles Classification is a Timely Issue

Notes from the Field

Measles Outbreak — Cook County, Illinois, October–November 2023
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On October 10, 2023, the Cook County Department of Public Health (CCDPH) in Illinois was notified by hospital A, a large pediatric facility, of a suspected measles case in a child aged 2 years (patient A) who had immigrated from Yemen on September 29 and who had no history of receipt of measles, mumps, and rubella (MMR) vaccine. The child visited hospital A’s emergency department (ED) on October 5 with fever, cough, and coryza and, after receipt of negative COVID-19, influenza, and respiratory syncytial virus test results, received
Measles Classification is a Timely Issue

Morbidity and Mortality Weekly Report

Public Health Actions to Control Measles Among Afghan Evacuees During Operation Allies Welcome — United States, September–November 2021

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Measles Virus (MeV)

Restricted Diversity Landscape, Impact on Molecular Surveillance/Classification
MeV Genome Organization

- N450 is widely acquired for typing and molecular surveillance.
- Virus is monotypic (canonically).
- Low substitution rates
Current Typing

Molecular typing was proposed in 1996, based on nucleoprotein.

Current genotyping uses 8 clades (A-H), with numeric designation of genotype (24 described in total).

Standard sequences (N450 and H) are well-described and available.

Use of named strains, human-curated.

Use of DSID (distinct sequence ID).

N450 is universally collected into controlled surveillance network data.

Other information that would be useful as sequences become less diverse:

- Lineage designation
- Relationship of sequence to others within a lineage
- Some representation of sequence identity
Pathogenesis: Restriction of Multiple Receptors

Lymphocyte (entry) – SLAM
Lung epithelium (exit) – Nectin 4

Epidemiology: Reduced Diversity of Circulating Types Over Time

Figure. Global distribution of measles virus genotypes,* 2016–2018

* The size of the circles reflects the numbers of replicates reported for each genotype.

Epidemiology: Reduced Diversity of Circulating Types Over Time

**FIGURE.** Global distribution of measles virus genotypes. Present Day

* The size of the circles reflects the numbers of replicates reported for each genotype.

Quasispecies and Structural Constraints

Granta: B-Lymphocyte (accumulates +G editing)
H358: Lung epithelial

**Elimination and Transmission Chain Discrimination**

**Measles elimination:** The absence of endemic measles virus transmission in a defined geographical area (e.g. region or country) for at least 12 months in the presence of a surveillance system that has been verified to be performing well.

**Chief Concern** - Maintain elimination by tracking a virus that is:

1. most contagious
2. structurally constrained,
3. genetically stable,
4. in an environment of decreasing diversity of circulating sequences
5. While using a large surveillance network with varying resources.
**Elimination and Transmission Chain Discrimination**

**Measles elimination:** The absence of endemic measles virus transmission in a defined geographical area (e.g. region or country) for at least 12 months in the presence of a surveillance system that has been verified to be performing well.

**Genetic homogeneity:** Overestimation of transmission chain length.
Multiple DSID Observed in Single Monophyletic Groups

1. MeV genetic classification is in **transition**.
2. Using N450 molecular clocks, many well-supported groups contain multiple DSIDs [colors].
3. Geographic and time information is reasonable for some of these groups.

Same color = Same DSID

Hyun Hwang, Personal Communication
Integration of Sequence Data in Outbreak Response
Measles virus transmission patterns and public health responses during Operation Allies Welcome: a descriptive epidemiological study


WGS was acquired for 43 of 47 cases.

Pertinent variables are shown if available.

Red arrow: Plausible transmission pairs.

Limits of resolution in scenarios of complex importation from genetically similar sequences.

Integration of Epidemiologic Linkage With Genetic Groupings

1. Geneticists and epidemiologists enter the same room and are forced to collectively interpret.

2. Payoff(s)
   1. Cross validation of datasets
   2. An (ultimately) more complete reconstruction of the infectious process.

Revising MeV Classification for Elimination Contexts

What are the major needs?

Heuristics

We cannot ask most labs in surveillance networks to perform Bayesian analyses.

Base-tree assignment methods are actively being investigated.

Use of Sparse and Multifactor Data

Cases are missed, linkage is uncertain (sparse genetic or linkage).

Validated Software, Models and Parameters

Well-described behavior, well-tested, well-integrated, well-maintained.

Revisions of MeV nomenclature

Ongoing in our laboratory. Standard MeV data is heavily controlled and reliable.

This additional information should be epidemiologically meaningful to approximate transmission lineages.
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The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.