



Wisconsin State
Laboratory of Hygiene

UNIVERSITY OF WISCONSIN-MADISON



Rice Lake

Kimberly

Madison

MAGICAL MYSTERY
TOUR

Get Back..... Global Resurgence of Measles

Erik Reisdorf, MPH, M(ASCP)

Team Lead-Virology

Communicable Disease Division



Key Learning Objectives

- Describe current situation in US and globally
- Historical perspective
- Review measles virus transmission
- MMR Vaccination
- Lab testing
- Review lab testing challenges
- Resources



Q: Does your institution routinely check immune status for measles?

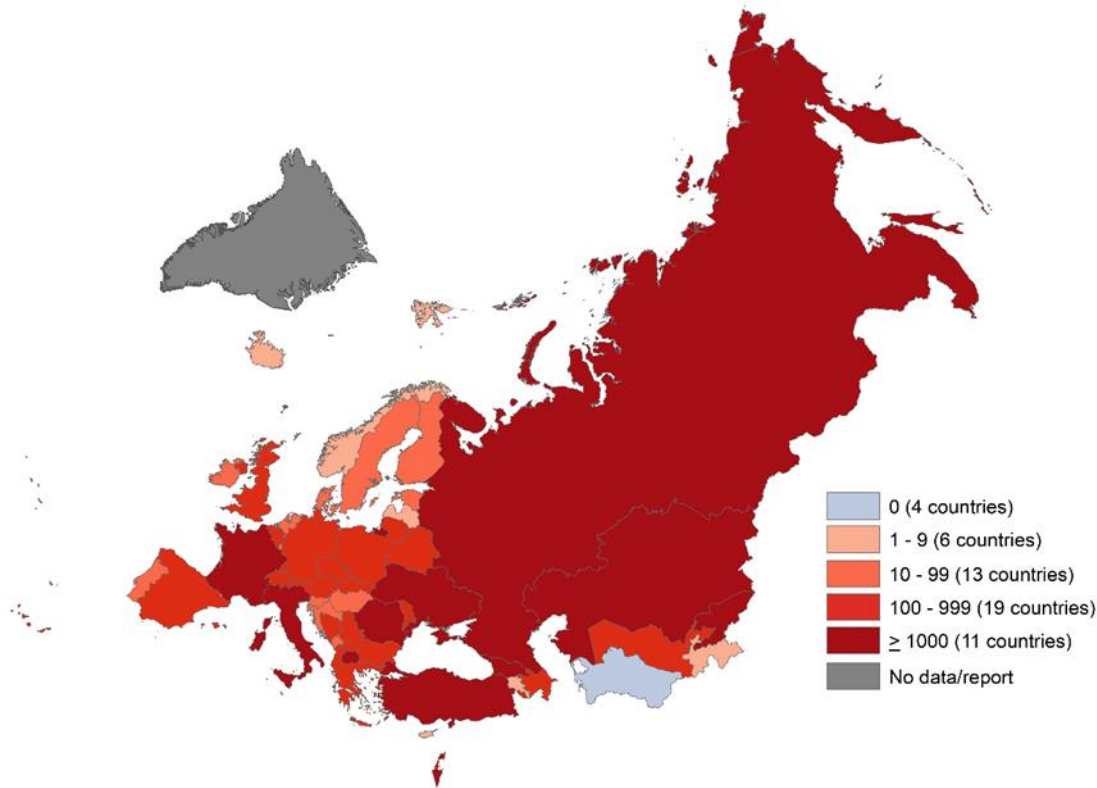
A) Yes

B) No



Current Situation (I)

Europe (May 2018-April 2019)



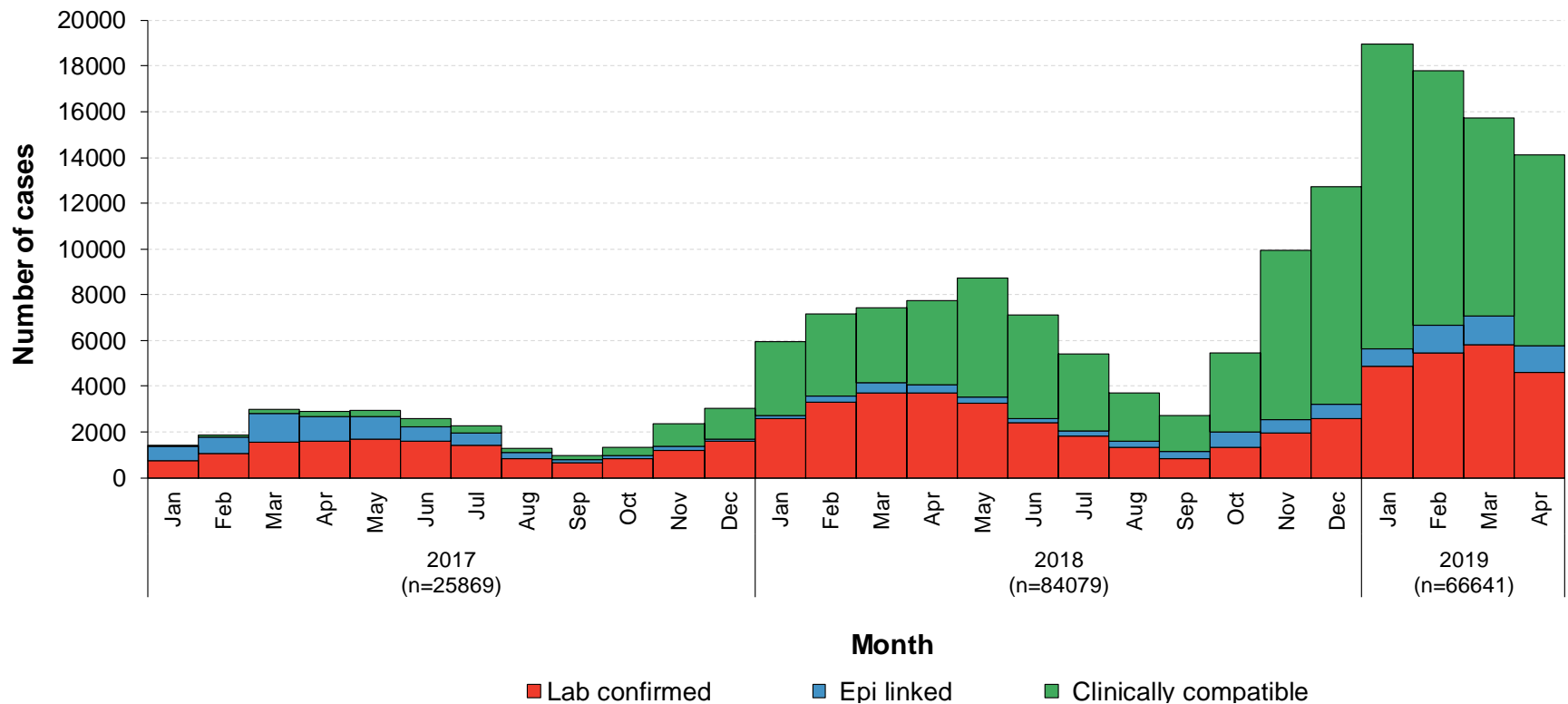
| Top 10 countries | |
|--------------------|-------|
| Country | Cases |
| Ukraine | 83533 |
| Kazakhstan | 7349 |
| Georgia | 4997 |
| Israel | 3886 |
| Kyrgyzstan | 2925 |
| Russian Federation | 2714 |
| Italy | 2138 |
| France | 1744 |
| Romania | 1387 |
| North Macedonia | 1370 |

Data source: WHO <http://www.euro.who.int/en/health-topics/disease-prevention/vaccines-and-immunization/publications/surveillance-and-data/who-epidata/who-epidata.-no.-52019>



Current Situation (II)

Measles cases by month in the WHO European Region, 2017–April 2019

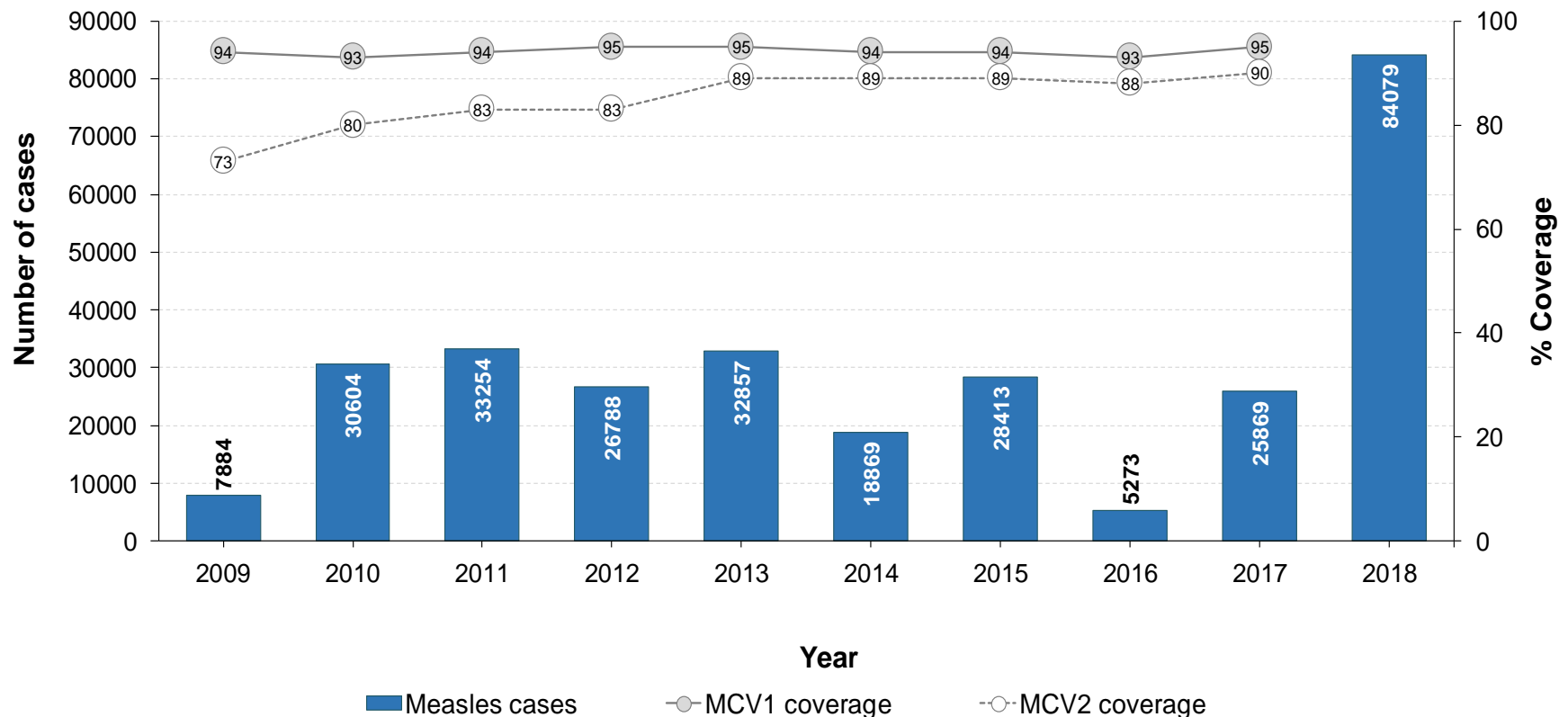


Data source: WHO <http://www.euro.who.int/en/health-topics/disease-prevention/vaccines-and-immunization/publications/surveillance-and-data/who-epidata/who-epidata-no.-52019>



Current Situation (III)

Measles cases, MCV1 and MCV2 coverage by year in the WHO European Region, 2009–2018



Data source: WHO <http://www.euro.who.int/en/health-topics/disease-prevention/vaccines-and-immunization/publications/surveillance-and-data/who-epidata/who-epidata.-no.-52019>



Measles, UK

- World Health Organization (WHO) stripped the UK (August, 2019) of its measles-free status, just 2 years after the country earned the designation.
- WHO had determined that measles transmission was re-established throughout the UK after 2018 saw 991 confirmed cases in England and Wales -- double the number of cases recorded in 2017.
- The same strain of measles virus was also detected in 2017 and 2018, which connotes established virus transmission .



Current Situation (IV)

Africa (Democratic Republic of Congo)



Key Challenges:

- Moving vaccine supplies to areas in need.
- Funding \$\$
- Cold chain maintenance
- Generators, fuel supply, refrigerators and transport needed.
- Ebola virus outbreak

- MSF reports a large scale outbreak of Measles.





Current Situation (V)



January to August
2019

| WHO Region | Member States Reported (expected) | Total Suspected | Total measles | Clinically confirmed | Epidemiologically Linked | Laboratory-confirmed | Data received |
|------------------------------|-----------------------------------|-----------------|---------------|----------------------|--------------------------|----------------------|----------------|
| African Region | 41 (47) | 192277 | 177542 | 23524 | 147465 | 6553 | 2019-08 |
| Region of the Americas | 32 (35) | | 2387 | 0 | 0 | 2387 | 2019-08 |
| Eastern Mediterranean Region | 20 (21) | 28852 | 15917 | 9952 | 2022 | 3943 | 2019-08 |
| European Region | 53 (53) | 98308 | 90012 | 53888 | 6088 | 30036 | 2019-08 |
| South-East Asia Region | 11 (11) | 53439 | 35778 | 25293 | 4604 | 5881 | 2019-08 |
| Western Pacific Region | 26 (27) | 110498 | 43175 | 35266 | 1276 | 6633 | 2019-08 |
| Total | 183 (194) | | 364811 | 147923 | 161455 | 55433 | 2019-08 |

For the current 2019 period, the WHO African Region has recorded a 900% (that is, a 10-fold) increase!!

Data Source: (preliminary WHO data)

https://www.who.int/immunization/monitoring_surveillance/burden/vpd/surveillance_type/active/measles_monthlydata/en/



Global Summary

- In the first six months of 2019, reported measles cases are the highest they have been in any year since 2006 (WHO, 2019).
- Globally, there have been almost three times as many cases reported to date in 2019 as there were at this same time last year (WHO, 2019).
- Major outbreaks are ongoing in Ukraine, DRC, Madagascar, Angola, Cameroon, Chad, Kazakhstan, Nigeria, Philippines, South Sudan, Sudan and Thailand.



Measles: Historical Perspective



Where did we start?

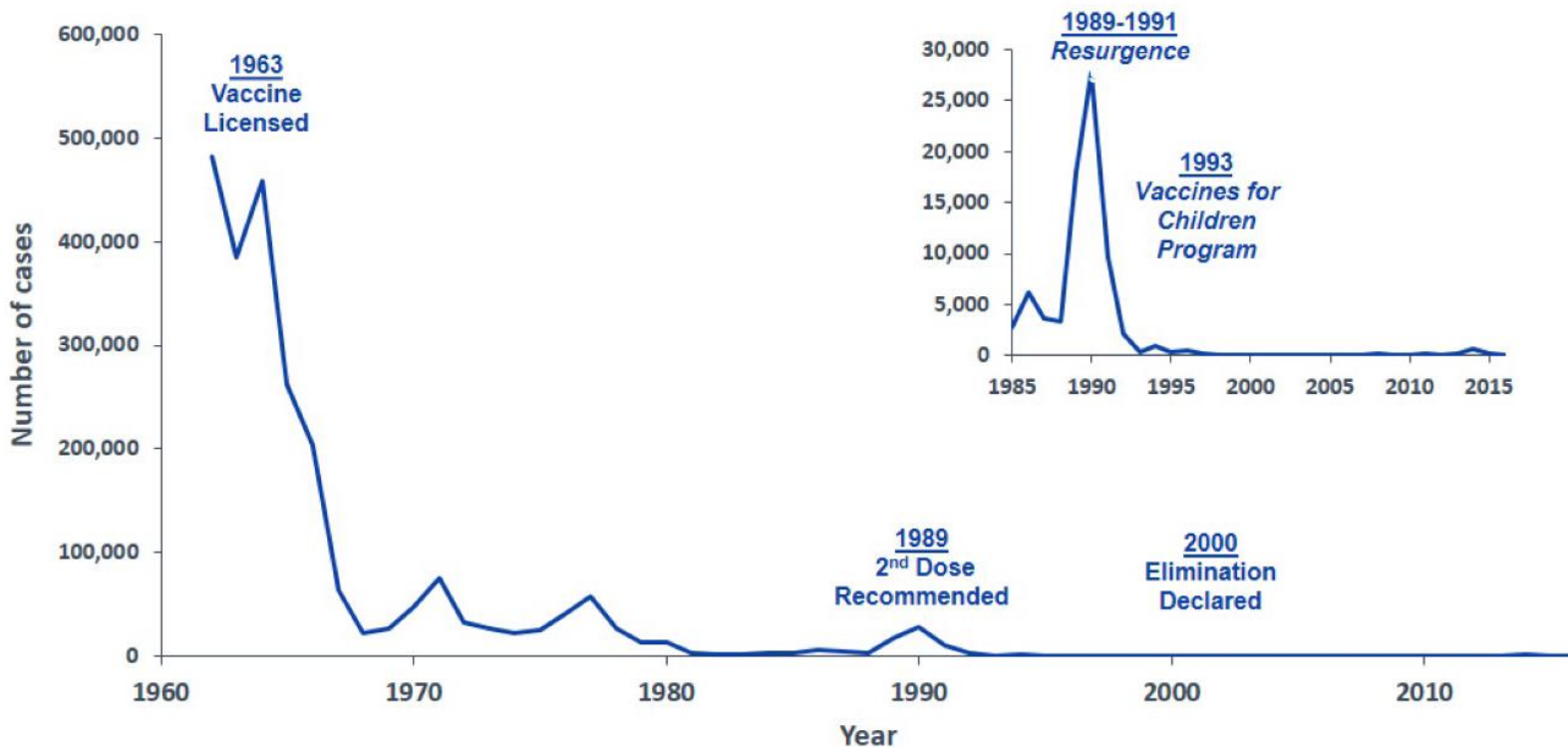
- Before measles vaccination program began in 1963, an estimated 3 to 4 million people contracted measles in the US.
- 48,000 annual hospitalizations
- 400 to 500 deaths per year.
- 1,000 cases developed encephalitis.

Data source: (CDC, 2019) <https://www.cdc.gov/measles/about/faqs.html>





Measles Cases, United States, 1962-2016*



*2016 data is preliminary and subject to change



Measles Virus Transmission

- Measles virus is found in the respiratory tract.
- Spread from coming into airspace of infected individual or contact with infected surfaces.
- Infectious period is **4 days BEFORE** rash appears and 4 days after.
- No other reservoir exists.
- Approximately 9-10% require hospitalization



Measles Complications

A specific feature of measles is a long-lasting immunosuppression due to the loss of immune memory B and T cells [Jiang et al, 2016].

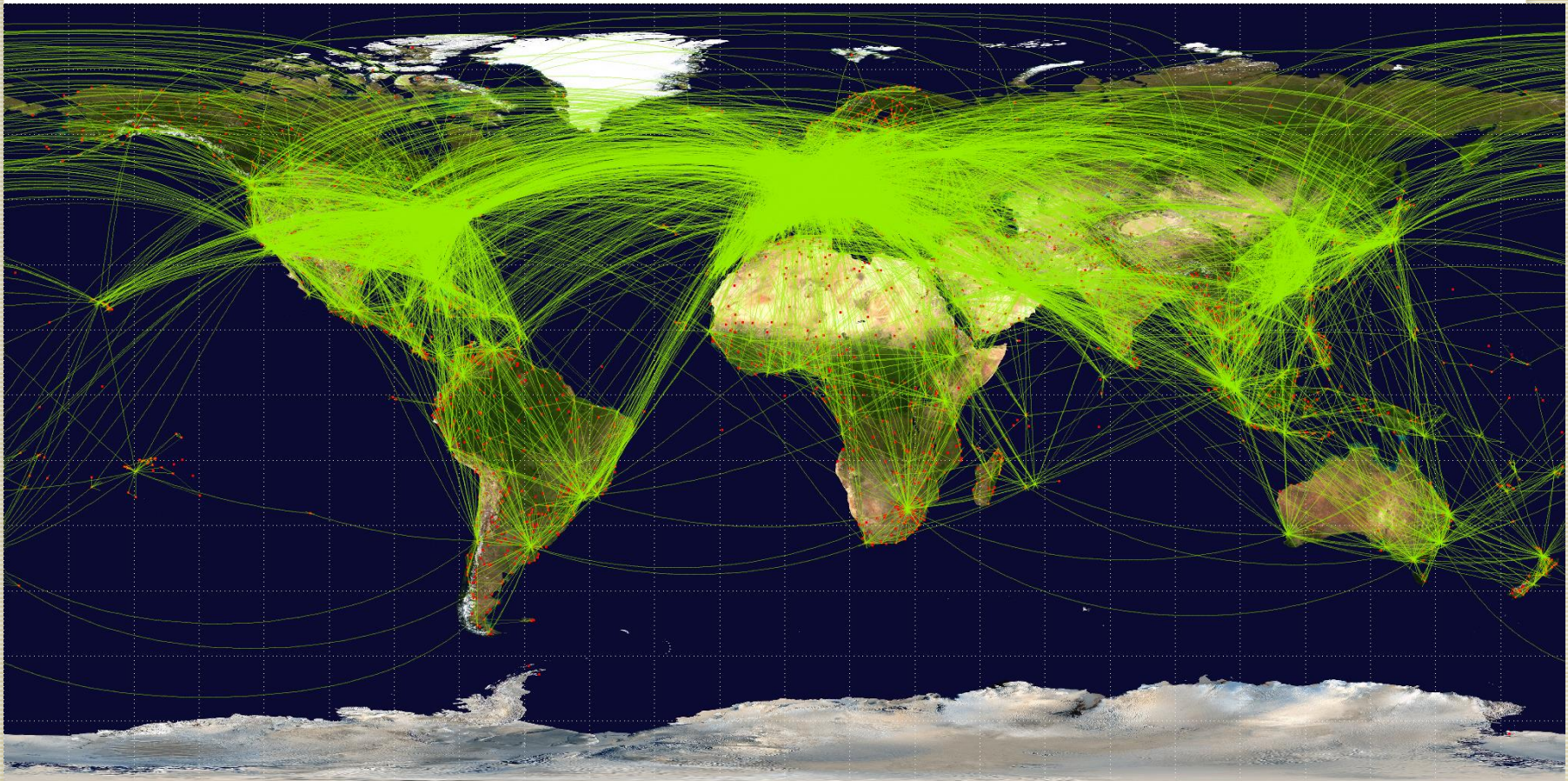
As a consequence, patients can encounter complications, especially in the setting of malnutrition in developing countries, ranging from bacterial superinfections, pneumonia, and diarrhea to postinfectious encephalomyelitis (PIE), or a sub-acute sclerosing panencephalitis (SSPE), **which can manifest even several years after recovery** [Jiang et al, 2016].



Measles was declared eliminated in North America so what happened?



The ever increasing connected world





Measles activity, United States

- International travel can contract measles when visiting popular EU countries.
- The CDC reports that 44 measles cases had been imported from January to April 2019 and **34 of 44 (77%)** were US residents traveling abroad.
- For effective measles “herd immunity”, community vaccination rate needs to be 95%





Measles vaccination, US

- Despite a national MMR vaccination coverage level of about 92%, one in 12 children in the U.S. is not receiving the first dose of MMR vaccine on time (CDC, 2019).
- Vaccination coverage continues to vary by state from 86% in some states to 96% in others (CDC, 2019). WI=89.9% (2017)
- ***Increases the number of susceptible persons.***
- Measles is *extremely contagious*....one person can infect up to 90% of close contacts lacking immunity!





Q2: Does your institution require evidence of MMR vaccination?

A) Yes

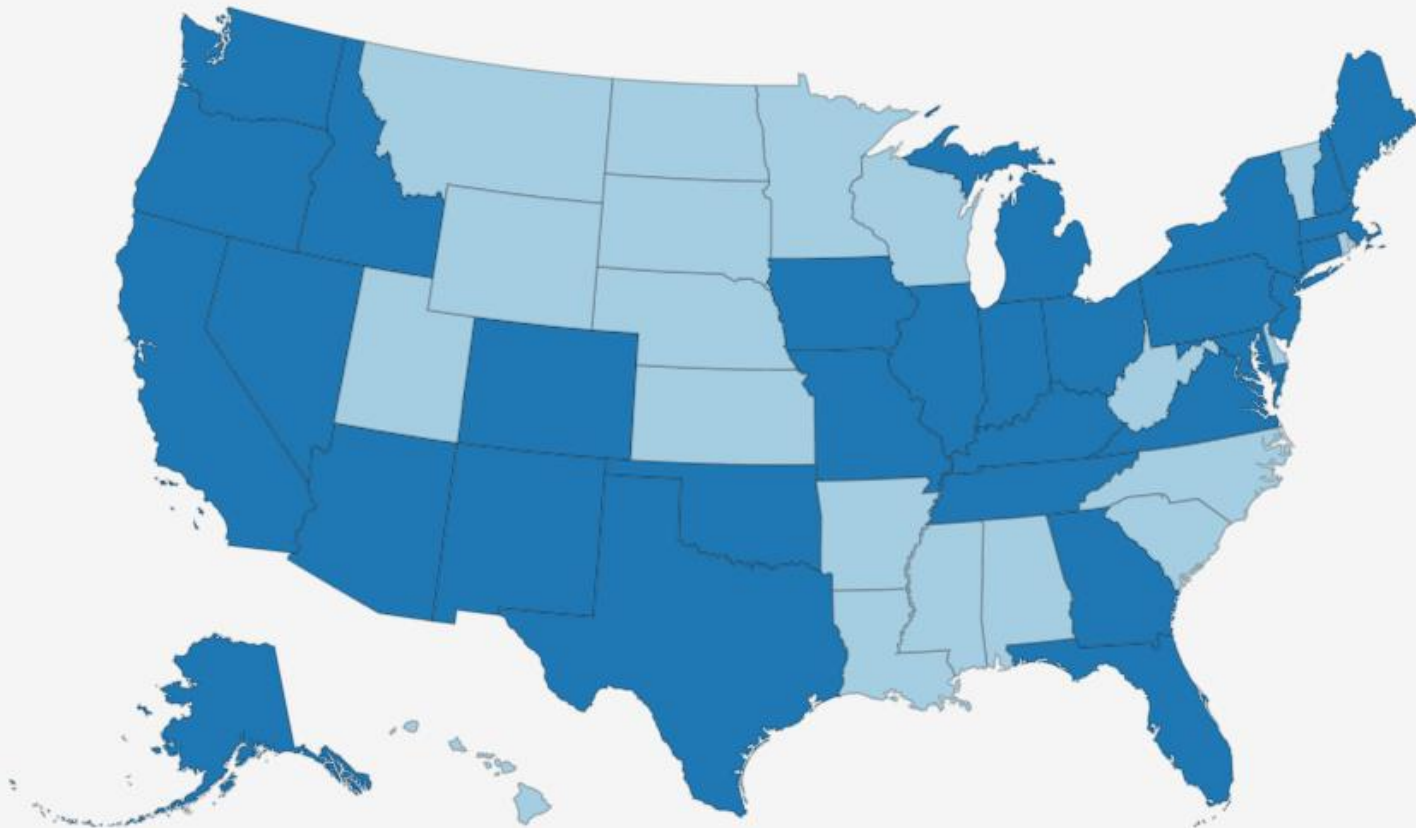
B) No

C) Considering



Measles activity, United States

- The United States has reported its highest measles case count in 25 years!
- In 2019, cases have occurred in 30 states

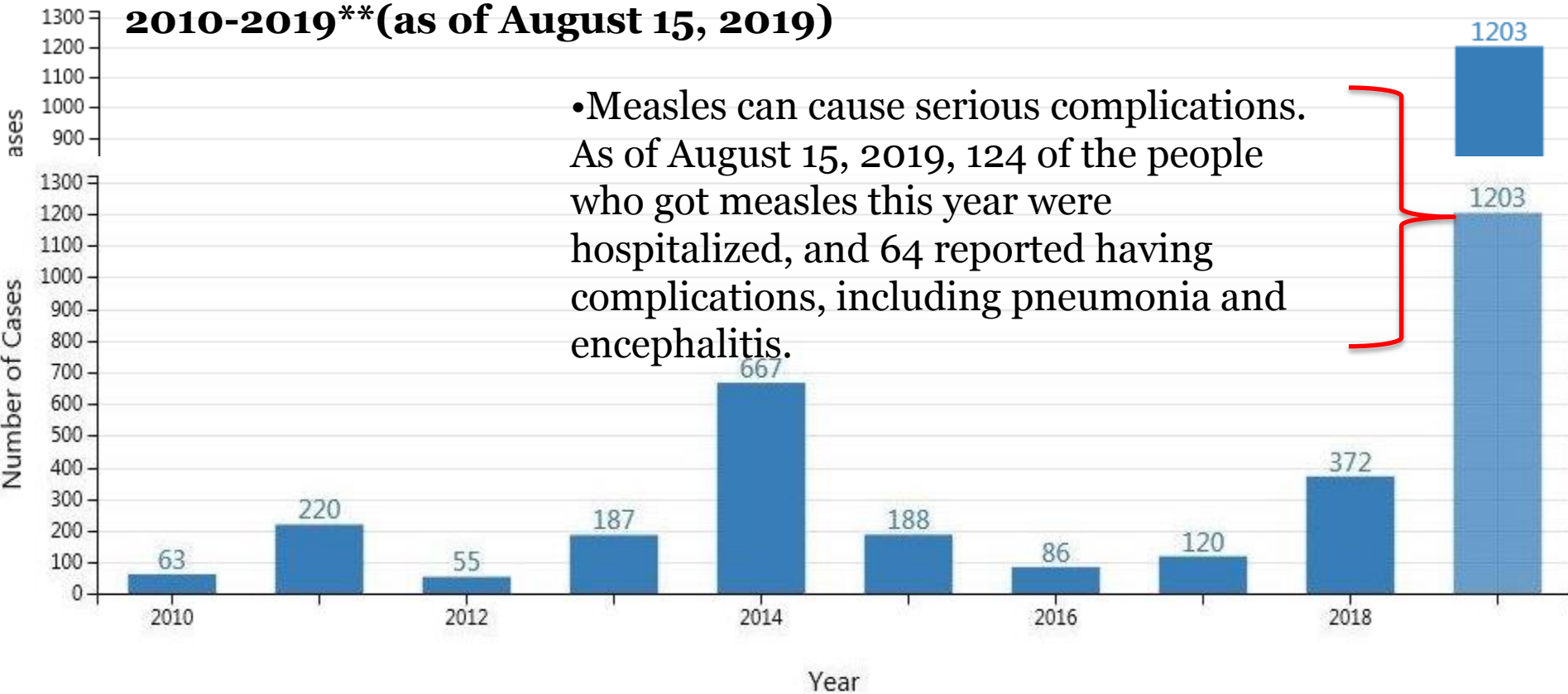




Measles activity, United States

Number of Measles Cases Reported by Year, US

2010-2019** (as of August 15, 2019)



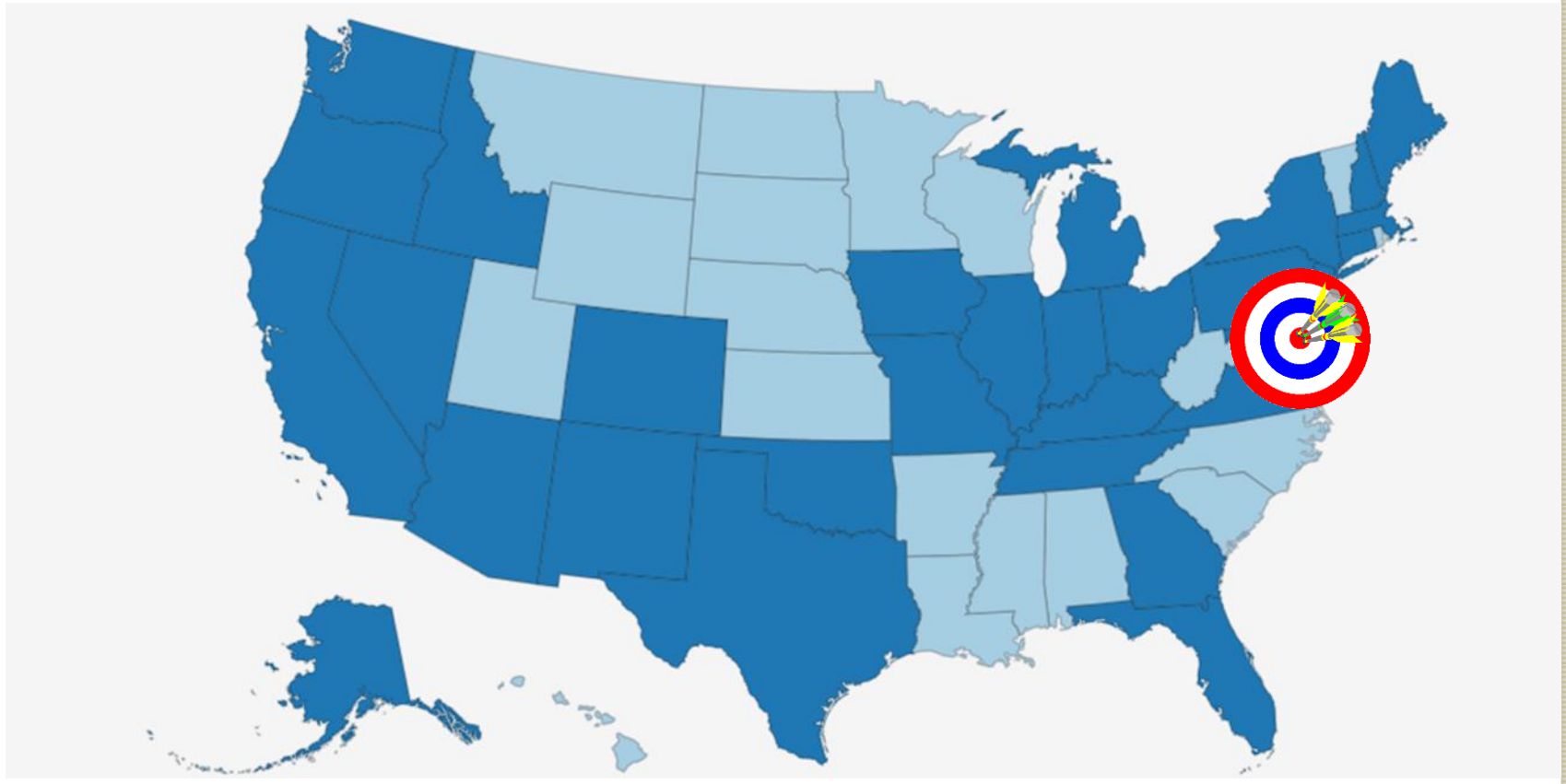
• Measles can cause serious complications. As of August 15, 2019, 124 of the people who got measles this year were hospitalized, and 64 reported having complications, including pneumonia and encephalitis.

Data Source (CDC, 2019) <https://www.cdc.gov/measles/cases-outbreaks.html>



Measles Activity, United States

New York, New Jersey





Measles Activity, NY

- The largest outbreak is in the Orthodox Jewish community of Brooklyn and Queens.
- As of 12 Aug 2019, the New York City Department of Health (NYC Health) confirmed 653 since September 2018.
- That outbreak, like most that have occurred in the USA this year (2019), has been linked to infected travelers from Ukraine and Israel.
- Genotypes include D8 and B3.

Source: CIDRAP (Center for Infectious Disease Research and Policy) [edited] <<http://www.cidrap.umn.edu/news-perspective/2019/08/us-measles-cases-top-1200-uk-loses-measles-free-status>>



MMR Vaccine

- Combination vaccine licensed in 1971
- 2 doses required to achieve maximum VE (starting at age 1)
- Safe (over 50 years of use)
- Highly effective





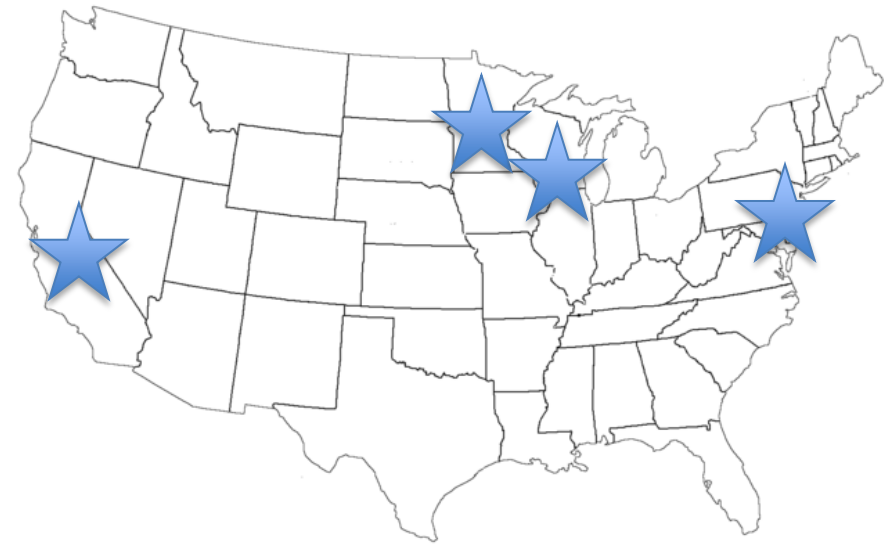
MMR Vaccine

- Composition: Live, attenuated measles, mumps and rubella virus
- Efficacy:
 - Measles: 93%-1 dose,
97% -2 dose
 - Mumps: 88% (2 doses)
 - Rubella: 95% or more (1 dose)
- Schedule: 2 doses

Vaccine Preventable Disease Reference Centers



- CDC/ APHL established 4 VPD RC's Network
- Testing performed with standardized SOP's
- Eight targeted priority pathogens.
- Aim to provide support for outbreak surge capacity and molecular epidemiology





Laboratory Testing: Measles

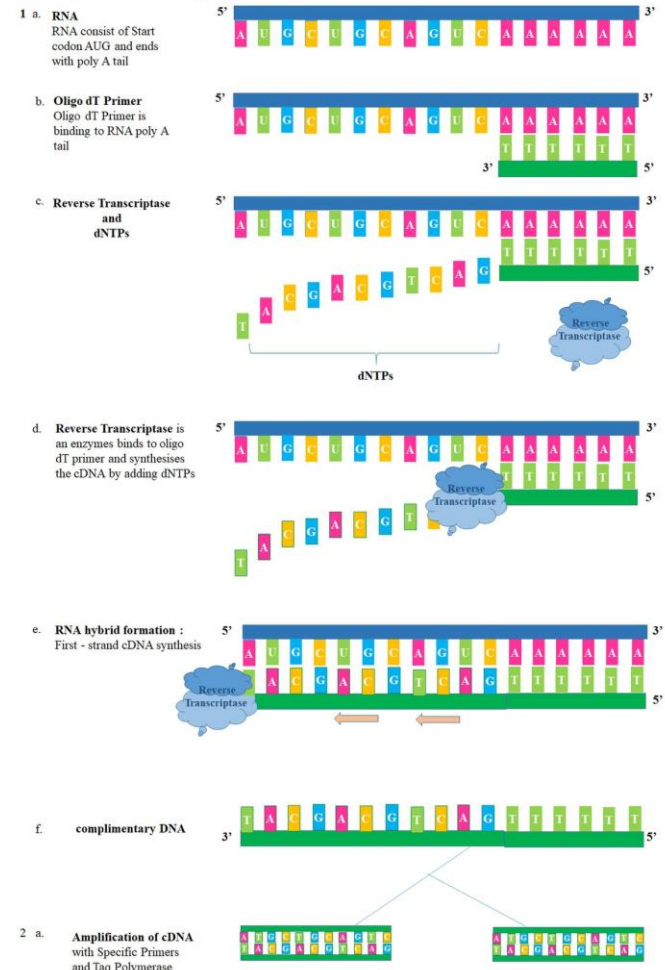




RT-PCR

4.8 Reverse transcription polymerase chain reaction (RT-PCR)

In RT-PCR, the RNA population is converted to cDNA by reverse transcription (RT), and then the cDNA is amplified by the polymerase chain reaction. The cDNA amplification step provides opportunities to further study the original RNA species, even when they are limited in amount or expressed in low abundances. Common applications of RT-PCR include detection of expressed genes, examination of transcript variants, and generation of cDNA templates for cloning and sequencing.



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- Pan-measles rRT-PCR
- Measles Vaccine rRT-PCR
 - Performed when recent immunization indicated.
 - Need immunization history

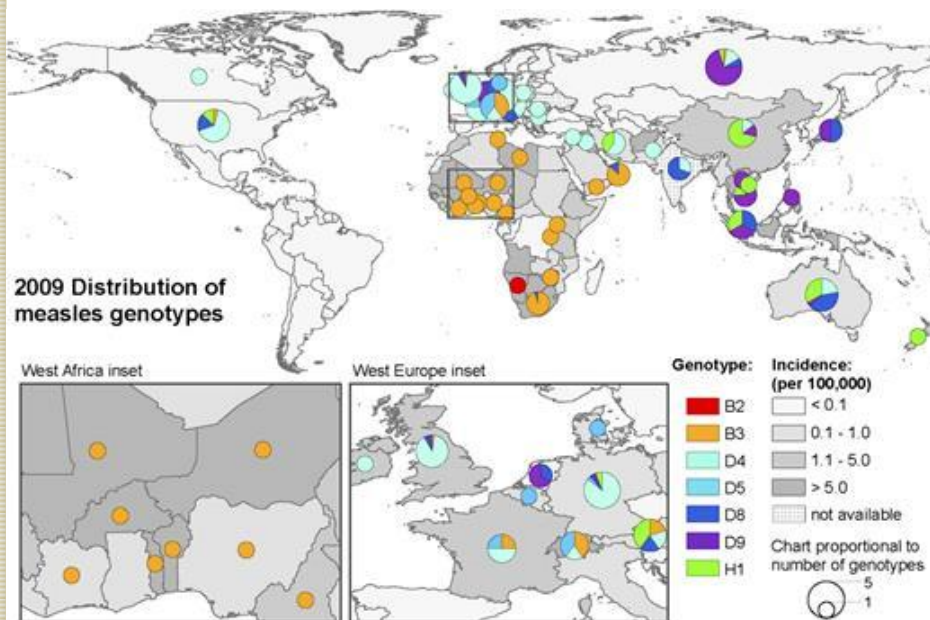
Specimen requirements:

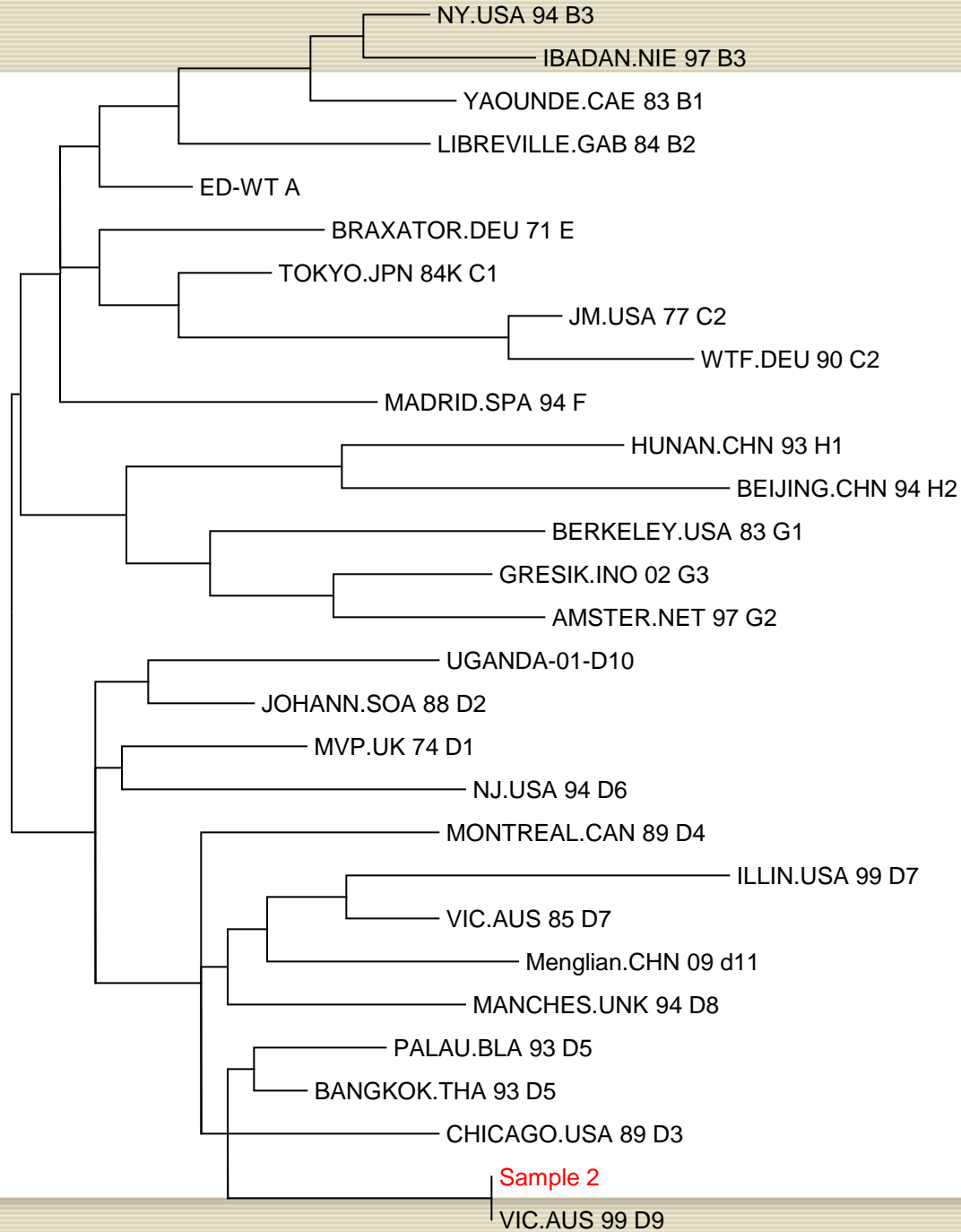
NP/Throat in VTM (+ urine if >7 days rash onset)



Genotyping

- Sanger sequencing (N gene)
- Primarily a tool for epidemiologic investigation.
- In the US, recent genotypes included D8 and B3







Serology

- Collect blood for IgM and IgG testing as soon as measles is suspected.
- Labs may need to be repeated if collected too early in illness.
- WSLH performs both tests (IgM IFA).





Measles Reporting

- All results are reported into WEDSS
- Usually reported by the end of the day in which they were resulted
- The Immunization Program is usually alerted to testing and results before they are entered into WEDSS



WSLH Customer Service: 800-862-1013

Wisconsin Immunization Program: 608-267-9959



Lab Testing Challenges

- Discriminate wild type and vaccine.
- Detection of vaccine strain (<3 weeks post vaccination).
- IgM false negative (first 72 hrs)
- Co-infections?





Measles by the numbers, WI

July 1, 2018 – June 30, 2019

- Pan-Measles RT-PCR 150
 - # Positive 11*
- Measles Vaccine RT-PCR 11
 - # Positive 11

No Wild Type Measles Virus detected in WI!





Resources

CDC

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

WI DPH Surveillance and Control Guide

<https://www.dhs.wisconsin.gov/publications/p00892.pdf>

Immunization Action Coalition

http://www.immunize.org/askexperts/experts_mmr.asp

