Modern Measles: Outbreaks and Complications

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R3 Talks

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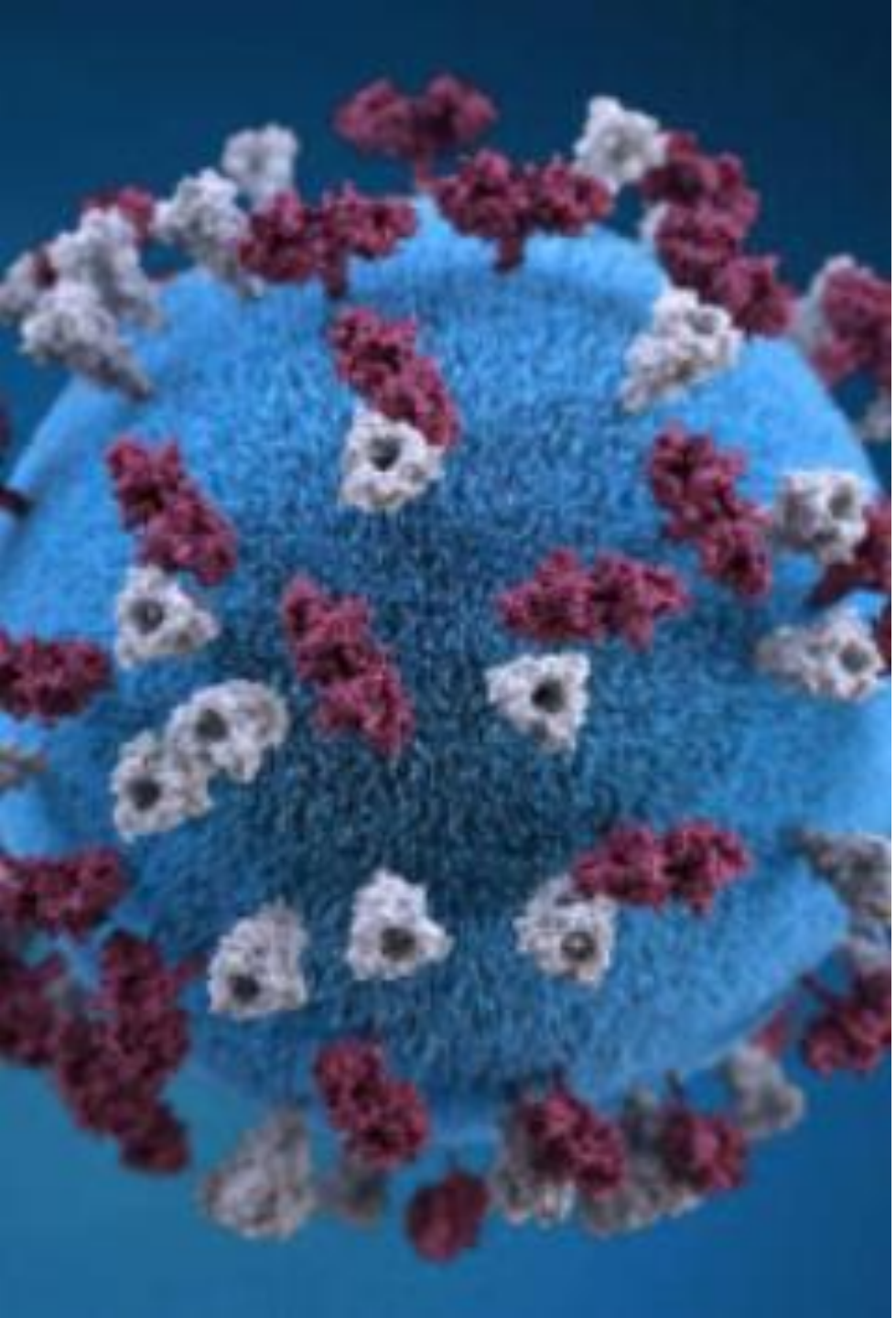
Objectives

- Review MMR vaccine and safety
- Understand evolving epidemiology of measles
- Discuss factors that have led to recent measles outbreaks
- Impact of COVID-19 pandemic on measles globally and implications for local community
- Review the presentation and possible complications in adults and other high risk populations
- Brief overview of diagnosis and treatment for high risk individuals



Measles

- Single stranded, enveloped RNA virus
- Transmission: one of most contagious infectious diseases
  - 9 out of 10 susceptible persons will develop
  - airborne spread and direct contact with infectious droplets
  - Remain infectious in air for up to 2 hours
- Incubation period: 11-12 days from exposure until 1st symptom

A Brief History

- Live Measles vaccine licensed in 1963
  - Decade prior:
    - Avg of 550,000 measles cases and 500 measles deaths reported annually
      - 48,000 people hospitalized and 1,000 people developed chronic disability from acute encephalitis annually
    - 3-4 million people infected with measles annually (most cases not reported)
- 2000: measles declared eliminated from the US
  - Absence of endemic measles virus transmission in a defined geographic area for 12 months or longer

Measles, Mumps, and Rubella Vaccine

https://doh.wa.gov

- Live attenuated vaccine
- Infants between 6-11 months traveling abroad should receive MMR prior
  - Should still receive 2 additional doses for long lasting protection

Vaccine Safety: Risks

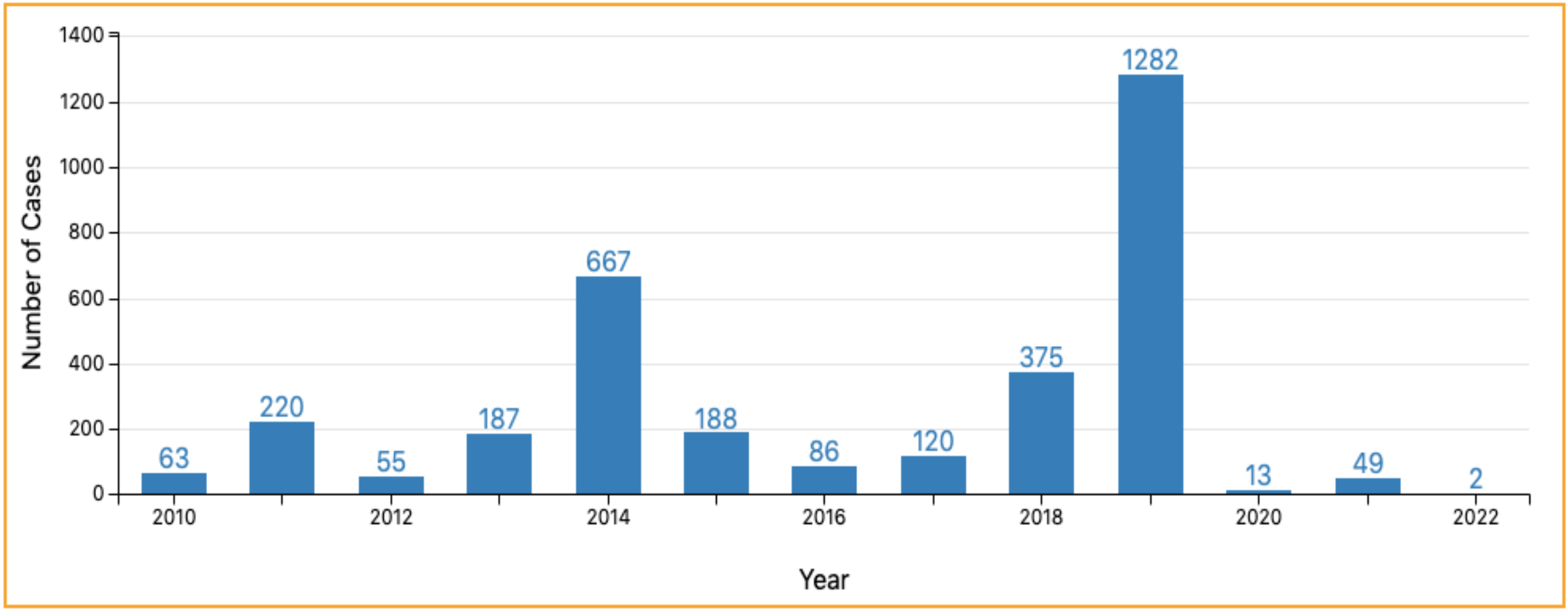
- Fever of 103F +
  - 5-15% of susceptible persons
  - 7-12 days following vaccination, lasts 1-2 days
- Transient rash
  - 5% of vaccine recipients
  - 7-10 days after vaccination
- Joint pain or stiffness
  - Up to 1 in 5 females past puberty and rubella nonimmune
  - 1-3 weeks after vaccination, lasts 2 days
- Febrile seizures
  - < 7 years 1 in 3,000 to 4,000 children
  - approx 6-14 days after vaccination
- Anaphylaxis
  - 1.8 to 14.4 cases per million doses
- Immune thrombocytopenia (ITP):
  - 1 case per 40,000 vaccinated children
  - Risk increased 6 weeks after vaccination
- Measles inclusion body encephalitis:
  - 3 published reports occurring in vaccinated people (immunocompromised)
  - 4-9 months after MMR vaccination

Vaccine Safety: Myths

- MMR does not contain mercury or thimerosal
- Per Global Advisory Committee on Vaccine Safety (GACVS): data does not suggest that measles vaccine can cause subacute sclerosing panencephalitis
- Numerous scientific studies have found no link between MMR vaccine and autism
  - Nov 2002 study by CDC and Danish Medical Research Council followed more than 500,000 children over 7 years. Published in NEJM

Number of measles cases reported by year

2010-2022* (as of April 29, 2022)



https://www.cdc.gov/measles/cases-outbreaks.html

A Closer Look at 2019

- January 1-October 1, 2019: total of 1,300 measles cases reported in 31 states
- Most cases associated with large and closely related outbreaks in NYC and NY state (total of 1,100 cases)
  - Orthodox Jewish communities
  - Both internationally imported (US traveler and foreign visitor)
- Three key risk factors for transmission of measles in this community
  - Pockets of low vaccination coverage/variable vaccine acceptance
  - Relatively high population density
  - Repeated importations of measles cases

Clark County Washington 2018-2019

- Since 2013, vaccination rates 10-14% lower that WA statewide average (88%)
- December 31, 2018 suspected measles case in unvaccinated 10 year old child who recently arrived from Ukraine
- As of March 28, 2019: 71 confirmed cases
  - Household: 51%
  - Public location (grocery store, retail, church): 25%
  - Child care center: 16%

School Exemption Law Change

- May 2019, WA state legislature passed a bill that removes personal and philosophical exemptions from MMR vaccine requirements
  - Applies to public + private schools and child cares
  - Employees must also provide proof of vaccination/immunity
  - Does not change religious and medical exemption laws for MMR
  - Does not change personal and philosophical exemptions for vaccines other than MMR.

Medical Exemptions are Rare

Contraindications	Precautions
• Severe allergic reaction (anaphylaxis) after previous dose or to a vaccine component • Pregnancy • Known severe immunodeficiency • Family history of altered immunocompetence	• Recent (<11 months) receipt of antibody containing blood product • History of thrombocytopenia or thrombocytopenic purpura • Needs for tuberculin skin testing of IGRA • Moderate or severe acute illness with or without fever

https://www.cdc.gov/vaccines/hcp/acip-recs/general-recs/contraindications.html

Outbreaks

- Increase in the number of travelers who get measles abroad and bring it into the US
  - Philippines, Ukraine, Israel, Thailand, England, France, Germany, and India
- Further spread of measles in US communities with pockets of unvaccinated people
  - Herd immunity: maintain ≥95% levels of age-appropriate vaccination coverage with 2 doses of MMR vaccine

Implications of COVID-19 Pandemic on Measles Globally

- Worldwide measles cases increased by 79% in first two months of 2022
  - From Jan-Feb 2022, 17,300 measles cases reported worldwide.
  - Versus 9,700 cases during first two months of 2021
- In 2020, 23 million children missed basic childhood vaccines
- Multifactorial:
  - Disruptions in routine immunizations services
  - Relaxed social distancing measures
  - Peoples displaced due to conflicts/crises in Ukraine, Ethiopia, Somalia, and Afghanistan
  - Lack of clean water and sanitation
  - Overcrowding

Top 5 countries with reported measles cases in the last 12 months, until April 2022 [1]

Country	Reported Measles cases	Rate per million cases	First dose measles coverage (%), 2019[2]	First dose measles coverage (%), 2020[3]
Somalia	9068	554	46	46
Yemen	3629	119	67	68
Afghanistan	3628	91	64	66
Nigeria	12 341	58	54	54
Ethiopia	3039	26	60	58

https://www.who.int/news/item/27-04-2022-unicef-and-who-warn-of--perfect-storm--of-conditions-for-measles-outbreaks--affecting-children

- As of April 2022: 21 large outbreaks globally in the last 12 months
- Majority due to insufficient measles vaccine coverage

Washington State: Refugees and Vaccination

- WA state: long history of welcoming refugees fleeing war and persecution
- In last 10 years, > 30,000 refugees from over 70 countries have resettled in WA state through U.S. Refugee Admissions Program
  - > 6,500 Ukrainians since 2010
    - 121 newly arrived individuals since October 2021
- Through WA involvement in Operation Allies Welcome:
  - > 3,200 Afghan arrivals since October 2021

https://www.dshs.wa.gov/esa/office-refugee-and-immigrant-assistance

Table A1: Vaccination coverage for the 19-35 month milestone vaccinations, June 2019-December 2021

Vaccine	Jun 2019	Dec 2019	Jun 2020	Dec 2020	Jun 2021	Dec 2021
Fully Vaccinated	66.4%	57.6%	62.0%	58.4%	61.2%	56.8%
DTaP (4)	74.6%	64.1%	69.2%	65.1%	68.3%	63.8%
Hib (3)	84.6%	75.6%	79.8%	75.4%	79.2%	74.9%
Polio (3)	84.8%	75.8%	80.4%	76.1%	80.1%	75.9%
HepB (3)	84.3%	75.0%	80.2%	75.9%	80.3%	76.2%
MMR (1)	85.3%	75.8%	80.6%	75.1%	78.7%	74.3%
Var (1)	83.0%	73.9%	78.6%	73.9%	77.5%	73.4%
PCV (4)	73.3%	65.0%	68.8%	64.8%	67.9%	63.4%

Table A4: Vaccination coverage for the 4-6 year milestone vaccinations, June 2019-December 2021

Vaccine	Jun 2019	Dec 2019	Jun 2020	Dec 2020	Jun 2021	Dec 2021
Fully Vaccinated	45.6%	44.1%	42.3%	42.6%	42.4%	41.7%
DTaP (5)	63.5%	59.5%	57.8%	57.2%	57.4%	56.6%
Hib (4)	66.8%	64.6%	63.1%	62.0%	61.9%	60.1%
Polio (4)	66.4%	62.0%	60.3%	59.4%	59.4%	58.5%
HepB (3)	87.5%	83.4%	83.4%	81.2%	81.6%	79.8%
MMR (2)	70.8%	66.5%	64.7%	63.1%	62.8%	61.8%
Var (2)	69.0%	65.1%	63.0%	62.0%	61.4%	60.5%
HepA (2)	76.8%	74.5%	73.7%	72.3%	72.4%	71.0%
PCV (4)	72.8%	70.9%	70.1%	69.2%	69.6%	68.3%

https://doh.wa.gov/sites/default/files/2022-05/348-867-ChildhoodImmunizationReport2019-2021.pdf

How does this impact us as providers?

- Perfect storm:
  - Decreasing vaccination rates + increasing refugee populations
- Likely to see increasing cases of measles in our local communities
- Important to be able to recognize presentation of measles and diagnosis
- Measles as a proxy
  - Concern for resurgence of other vaccine preventable diseases

Presentation: Prodrome

- Lasts 2-4 days (can be up to 8 days)
- Fever (Tmax 105F), malaise, and anorexia
- Three "C's"
  - Cough, coryza, and conjunctivitis
- Koplik spots: 24-48 hours before rash
  - clustered, white lesions on buccal mucosa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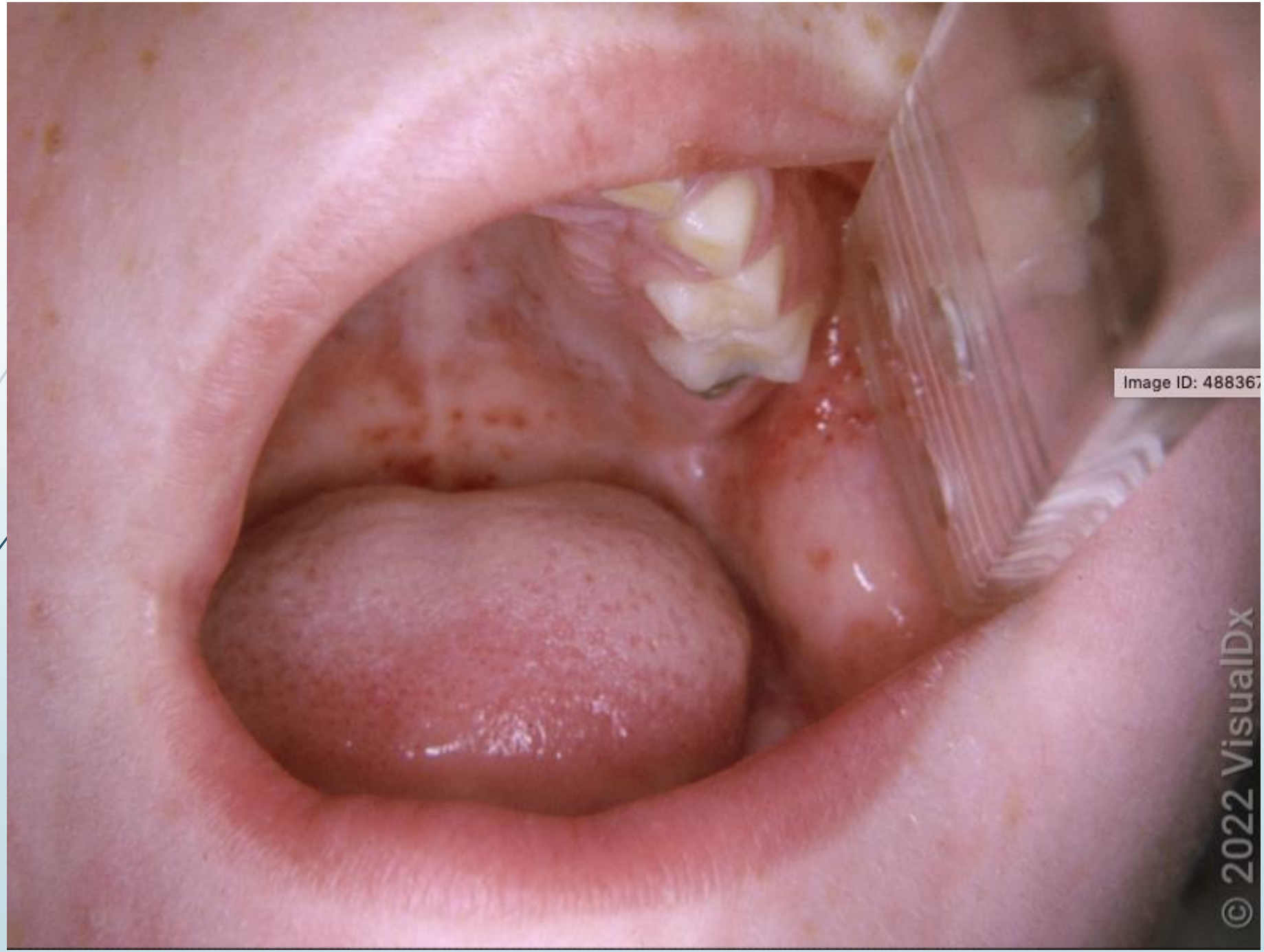
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Presentation: Rash

- Maculopapular rash
  - 14 days after exposure
  - Spreads from head >> trunk >> lower extremities
  - After 3-4 days rash darkens to brownish color then fades
  - Fine desquamation in severe areas
  - Ordinarily lasts 5-6 days
  - Contagious 4 days before to 4 days after rash appears


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Diagnosis

- Consider in those with classic presentation
  - Recently travelled or exposed to person with febrile rash illness
- Confirming measles infection with BOTH:
  - Serum: measles-specific IgM antibody
  - Throat/nasopharyngeal swab: measles RNA by real-time polymerase chain reaction (RT-PCR)
- Urine sample can also contain virus
  - Increase likelihood of detecting the virus
- Molecular analysis to detect measles genotype
  - Helpful in mapping transmission pathways

Legal Reporting Requirements

- **Health care providers + Facilities:**
  - *immediately* notifiable to local health jurisdiction
- **Laboratories:**
  - *immediately* notifiable to local health jurisdiction
  - specimen submission required - isolate or clinical specimen associated with positive result (2 business days)
- **Local health jurisdictions:**
  - *immediately* notifiable to Washington State Department of Health (DOH) Communicable Disease Epidemiology (CDE).

Health

Measles

County

Case name (last, first) _____
Birth date ___/___/___ Sex at birth ☐ F ☐ M ☐ Other Alternate name _____
Phone _____ Email _____
Address type ☐ Home ☐ Mailing ☐ Other ☐ Temporary ☐ Work
Street address _____
City/State/Zip/County _____
Residence type (incl. Homeless) _____ WA resident ☐ Yes ☐ No

ADMINISTRATIVE

Investigator _____
LHJ Case ID (optional) _____
LHJ notification date ___/___/___
Classification ☐ Classification pending ☐ Confirmed ☐ Not reportable ☐ Probable ☐ Ruled out ☐ Suspect
Investigation status
☐ In progress
☐ Complete
☐ Complete – not reportable to DOH
☐ Unable to complete Reason _____
Investigation start date ___/___/___
Investigation complete date ___/___/___
Case complete date ___/___/___
Outbreak related ☐ Yes ☐ No
LHJ Cluster ID _____ Cluster Name _____

DEMOGRAPHICS

Age at symptom onset _____ ☐ Years ☐ Months
Ethnicity ☐ Hispanic or Latino ☐ Not Hispanic or Latino ☐ Unk
Race (check all that apply) ☐ Unk ☐ Amer Ind/AK Native ☐ Asian ☐ Black/African Amer ☐ Native Hi/other PI ☐ White ☐ Other _____
Primary language _____
Interpreter needed ☐ Yes ☐ No ☐ Unk
Employed ☐ Yes ☐ No ☐ Unk Occupation _____
Industry _____ Employer _____
Work site _____ City _____
Student/Day care ☐ Yes ☐ No ☐ Unk
Type of school ☐ Preschool/day care ☐ K-12 ☐ College ☐ Graduate School ☐ Vocational ☐ Online ☐ Other
School name _____
School address _____
City/State/County _____ Zip _____
Phone number _____ Teacher's name _____

REPORT SOURCE

Initial report source _____
LHJ _____
Reporter organization _____
Reporter name _____
Reporter phone _____
All reporting sources (list all that apply)
_____
_____
_____

COMMUNICATIONS

Primary HCP name _____
Phone _____
OK to talk to patient (if Later, provide date)
☐ Yes ☐ Later ___/___/___ ☐ Never
Date of interview attempt ___/___/___
☐ Complete ☐ Partial ☐ Unable to reach
☐ Patient could not be interviewed
Alternate contact ☐ Parent/Guardian ☐ Spouse/Partner ☐ Friend ☐ Other _____
Name _____ Phone _____

CLINICAL INFORMATION

Complainant ill ☐ Yes ☐ No ☐ Unk Symptom Onset ___/___/___ ☐ Derived Diagnosis date ___/___/___
Illness duration _____ ☐ Days ☐ Weeks ☐ Months ☐ Years Illness is still ongoing ☐ Yes ☐ No ☐ Unk

Clinical Features

Y N Unk
☐ ☐ ☐ **Fever** Temp measured? ☐ Yes ☐ No Highest measured temp _____°F Onset ___/___/___ Duration _____ days
☐ ☐ ☐ **Rash (any)** Onset ___/___/___ Duration _____ days
Where did it first appear ☐ Head ☐ Chest ☐ Abdomen ☐ Upper extremities ☐ Lower extremities ☐ Back ☐ Other _____
☐ ☐ ☐ Rash progression: spread downward
Distribution ☐ Generalized ☐ Localized ☐ Unk
☐ ☐ ☐ **Conjunctivitis** Onset ___/___/___
☐ ☐ ☐ **Coryza (runny nose)** Onset ___/___/___
☐ ☐ ☐ **Cough** Onset ___/___/___
☐ ☐ ☐ Diarrhea *(3 or more loose stools within a 24 hour period)*
☐ ☐ ☐ Encephalitis or encephalomyelitis
☐ ☐ ☐ **Koplik spots**
☐ ☐ ☐ Lymphadenopathy Location ☐ Postauricular ☐ Other cervical ☐ Generalized ☐ Unk ☐ Other

Measles required variables are in **bold.** Answers are: Yes, No, Unknown to case

DOH 210-073(Rev. 11/2019)

Post exposure prophylaxis (PEP)

- Exposed to measles with uncertain immunity
- Administer MMR vaccine within 72 hours of initial exposure
- OR immunoglobulin (IG) within 6 days of exposure
- DO NOT administer MMR vaccine + IG simultaneously
  - Invalidates the vaccine

Treatment

- No specific antiviral
- Supportive management
- Vitamin A: severe measles
  - Administered upon diagnosis and repeated the next day
    - < 6 months: 50,000 IU
    - 6-11 months: 100,000 IU
    - > 12 months: 200,000 IU
- Ribavirin: treatment of measles pneumonia
  - Patients < 12 months or patients > 12 months requiring ventilator support
  - Immunosuppressed

Complications

- Measles can cause immune suppression and secondary infections
- Common
  - Diarrhea: 8% of cases
  - Otitis media: 5-10%, younger individuals
  - PNA: 6%
  - Croup, bronchiolitis, and bronchopneumonia
- Serious illness: requiring hospitalization
  - 1 out of every 1,000 cases
  - Death from respiratory or neurologic complications:
  - Acute encephalitis:
    - Permanent brain damage

Acute disseminated encephalomyelitis

- Demyelinating disease: post infectious autoimmune response
  - 1 in 1,000 measles cases
- Recovery phase: within 2 week of the exanthem
- Clinical presentation: fever, headache, neck stiffness, seizures, and confusion
- Associated with 10-20% mortality
- In survivors, neurologic abnormalities common
  - Behavioral disorders, cognitive deficits, and epilepsy

Subacute sclerosing panencephalitis

- Progressive degenerative disease of CNS: rare and fatal
- Occurs 7-10 years after infection
- Risk factor: measles infection at an early age (< 2 years)
- Unclear pathogenesis
  - Related to persistent infection with a genetic variant within the CNS
- Divided into stages:
  - Stage I: insidious dev of neuro symptoms (personality changes, strange behavior, lethargy). Weeks to years
  - Stage II: classic myoclonus w/massive jerks q 5-10 seconds and worsening dementia. 3 to 12 months
  - Stage III-IV: further neurologic deterioration. Flaccidity and autonomic dysfunction. Leading to vegetative stage

High Risk Individuals

- Infants and children < 5 years
- Older adults
- Pregnant individuals
- Immunocompromised
- Vitamin A deficient/poor nutritional status

Immunocompromised

- Defects in cell mediated immunity
- Presentation can be atypical and variable
  - Exanthem absent, fade quickly , or severe with desquamation
  - Purpura
- High suspicion in immunocompromised patient who presents with PNA or encephalitis despite history of immunization
- Giant cell pneumonia: multinucleated giant cells in lung tissue
- Measles inclusion body encephalitis: 1-6 months after exposure
  - Seizures, AMS, and myoclonus

Pregnant Individuals

- Increased risk for maternal and fetal complications
  - Low birthweight, spontaneous abortion, intrauterine fetal death, premature birth, and maternal death
- Common complications
  - Diarrhea (60%), PNA (40%), and encephalitis (5%)

Questions?

References

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