Measles

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Objectives

- Review the history and epidemiology of Measles in the United States.
- Review the development and impact of Measles Vaccination.

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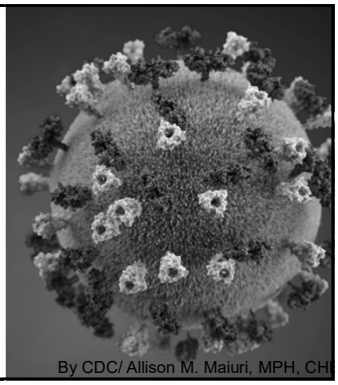
What is Measles?

- *Morbillivirus hominis* – single stranded RNA virus from *Paramyxoviridae* family
  - Exclusive human pathogen
  - Closest relative: cattle pathogen Rinderpest morbillivirus
  - Molecular studies suggests divergence and establishment in 6th century BCE



By CDC/ Allison M. Maiuri, MPH, CHES

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What is Measles?

Airborne

Highly Contagious

R0 of 12-18

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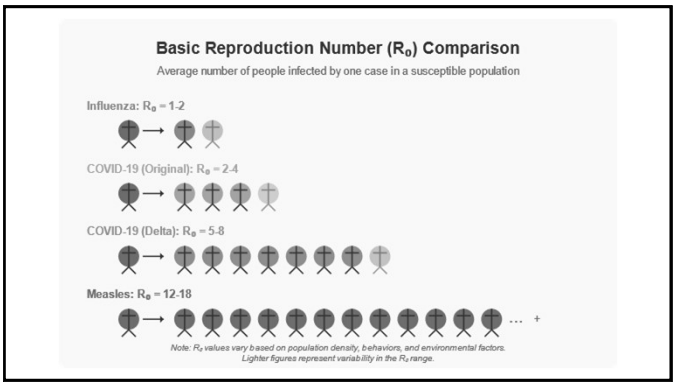

Epidemiology

Worldwide, Source: WHO

Prior to vaccine, 2.6 million deaths a year

2023: 10.3 million cases and 107,500 deaths

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Epidemiology

- Ubiquitous childhood disease before vaccine
  - US: 3-4million cases/year
  - 450 deaths/year
  - Complications occur in 3 in 10 who get measles.

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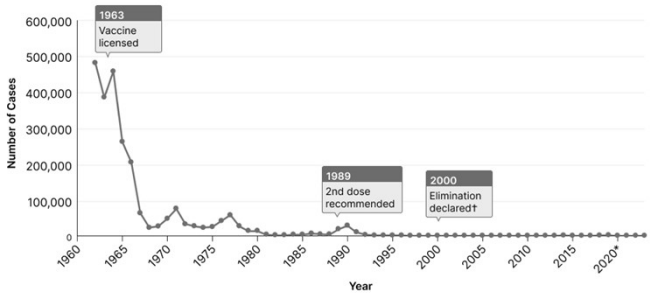
Reported Measles Cases in the United States from 1962 – 2023*

Source: CDC



Vaccine Development

In US history

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Measles Vaccine Timeline in the United States

1950s Early Research | 1960s First Vaccines | 1970s MMR Launch | 1980s-1990s Elimination Efforts | 2000s Elimination Achieved | 2010s-2020s Challenges

1950s: Early Research & Development

- **1954**: Dr. Thomas Peebles isolates the measles virus from the blood of a student named David Edmonston.
- **1958**: Drs. John Franklin Enders & Sam Katz began developing a live attenuated vaccine using the Edmonston-B strain.

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Measles Vaccine Timeline in the United States

1950s Early Research | 1960s First Vaccines | 1970s MMR Launch | 1980s-1990s Elimination Efforts | 2000s Elimination Achieved | 2010s-2020s Challenges

1960s: Initial Vaccines and Licensure

- **1963**: The first measles vaccines are licensed in the US
  - Edmonston B strain (live attenuated)
  - A killed (inactivated) vaccine is licensed but later withdrawn
- **1968**: Improved Edmonston-Enders strain (formerly Moraten) vaccine is licensed and becomes the standard measles vaccine used in the US

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Measles Vaccine Timeline in the United States

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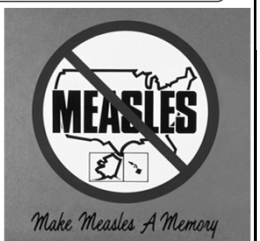
1970s: Combination Vaccines and Campaign Launch

- **1971**: The combined measles-mumps-rubella (MMR) vaccine is licensed in the US
- **1978**: The US government announces a goal to eliminate measles from the country by 1982



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Measles Vaccine Timeline in the United States

1980s-1990s: Elimination Efforts and Resurgence

- **1989-1991**: Major measles resurgence with over 55,000 cases and 123 deaths
- **1989**: ACIP, AAP, AAFP all recommend a 2nd dose of MMR vaccine for all children
- **1998**: "The Lancet" publishes a fraudulent research paper linking the MMR vaccine and Autism without any robust scientific evidence.

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Measles Vaccine Timeline in the United States

2000s: Elimination Achievement and Maintaining Status

- **2000**: Measles declared eliminated from the United States (defined as absence of continuous disease transmission for 12 months)
- **2005**: MMRV vaccine (ProQuad) licensed by FDA
- **2010**: "The Lancet" retracts fraudulent paper & lead author Andrew Wakefield is banned from practicing medicine.

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Current Measles Vaccine

- In US: available in MMR and MMRV formulations
  - MMR: 6 months & older
  - MMRV: 12 months to 12 years
- Routine schedule in US:
  - 1st dose: 12-15 months
  - 2nd dose: 4-6 years

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Vaccine details

- **Adverse reactions**
  - Fever (up to 15%)
  - Rash (up to 5%)
  - Febrile seizure (rare: 1 in 3000-4000)
  - Thrombocytopenia (rare: 1 in 40,000)
  - Anaphylaxis (rare: 2-14 in 1 million)

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Epidemiology

- **2001-2015**: Most US cases are imported from unvaccinated foreign travelers
  - Local outbreaks (3 or more cases) occur when infected traveler spreads to their community
  - Median 28 imported cases/yr
  - 90% imported measles is vaccine-preventable

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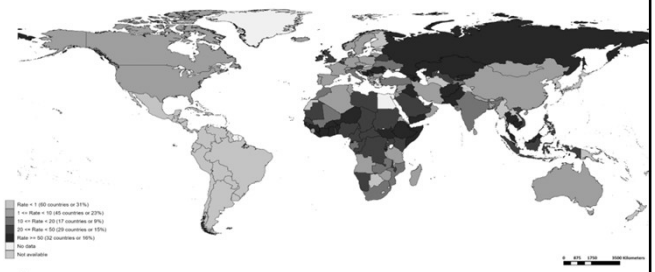
Measles Incidence Rate per Million (12M period)

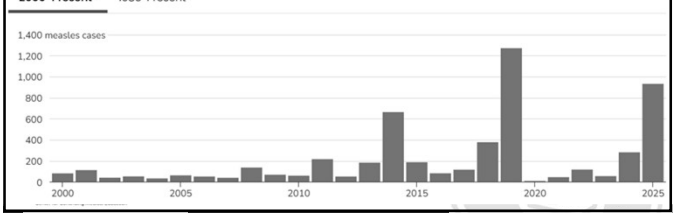


Epidemiology

Yearly measles cases

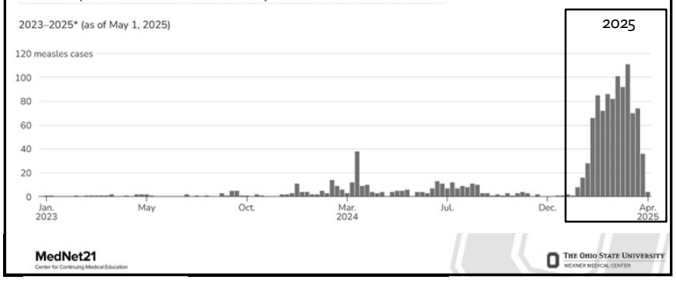
as of May 1, 2025

2000–Present* 1985–Present*



Epidemiology

Weekly measles cases by rash onset date



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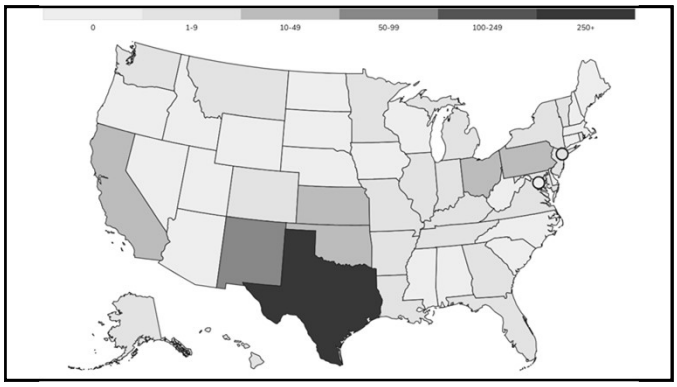

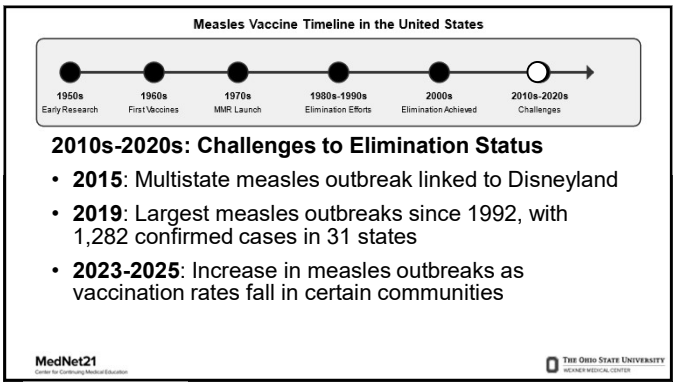

Presumptive immunity

- Birth before 1957 (when measles was endemic)
- Laboratory confirmation of:
  - Prior measles disease
  - Immunity (positive IgG)
- ***Written*** documentation of vaccination

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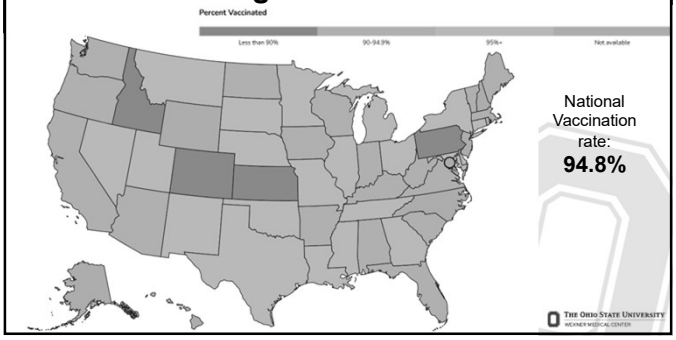
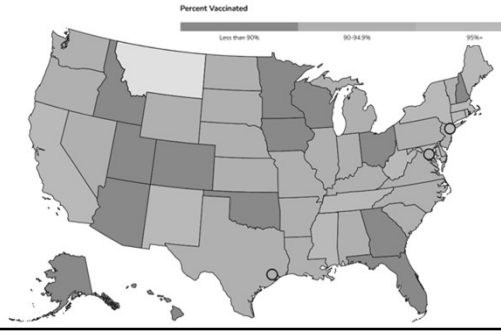
2011-12 Kindergarten vaccination rates



2023-24 Kindergarten vaccination rates



National Vaccination rate:
92.7%

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Measles

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Disclosures

- I have no conflicts of interest to disclose relevant to today's presentation

Objectives

1. Identify the clinical features and complications of measles, such as prodromal symptoms and the characteristic rash phase.
2. Describe the diagnostic methods, current management strategies, and preventive measures to control outbreaks

Outline

- Pathophysiology
- Clinical Presentation
- Diagnosis & Management
- Prevention
- Common Clinical Questions

Measles Pathophysiology

Pathophysiology

- Virus contained in respiratory droplets or aerosols initially infect dendritic cells and macrophages associated with the conjunctiva & respiratory tract
  - Highly contagious due to airborne transmission route as well as very low infectious dose
- Measles virus disseminates to lymphoid tissue, which are the major sites of viral replication
  - Bone marrow, thymus, spleen, tonsils, lymph nodes
- Leads to widespread infection of both B- and T-cells

Pathophysiology

- Following replication, measles virus spreads systemically to the respiratory tract, GI tract, kidney, liver, and skin
  - The viremia and dissemination across organ systems leads to fever and onset of systemic symptoms
  - Respiratory epithelial cells become infected and shed virus into mucus, which is expelled via coughing
- Onset of rash corresponds with resolution of viremia
  - Rash occurs as a response to infected dermal endothelial cells which are subsequently cleared by cellular immune response

Immune Consequences

- Virus efficiently replicates in lymphoid tissue
- Results in extensive decrease in memory B- and T-cells
  - Lymphopenia and measles-associated immune suppression
- Lymphopenia slowly resolves within 1 week of viral clearance
  - Functional impairment of immune system may last months to years and lead to increased rates of secondary infection

Clinical Presentation

Clinical Presentation

- Incubation period averages 10-12 days (range: 7-21)
- Symptomatic stage considered as two distinct periods:
  - Prodromal phase (2-4 days prior to rash onset)
    - Onset of fever, rhinitis, tracheobronchitis, and conjunctivitis
      - Note: Conjunctivitis may be absent in up to 1 in 3
    - Appearance of Koplik spots ~1 day prior to rash
      - Note: Koplik spots may be absent in up to 1 in 3
    - Other symptoms: headache, photophobia, pharyngitis, abdominal pain, generalized lymphadenopathy

Koplik Spots

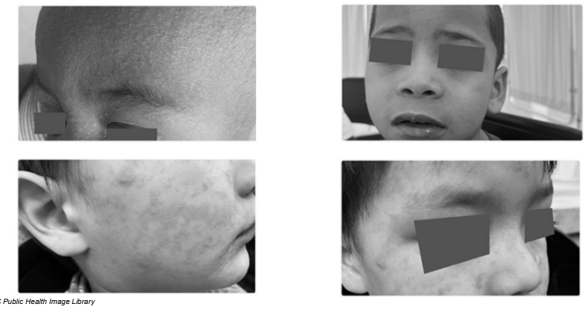
CDC Public Health Image Library

Small, red, irregularly-shaped spots with blue-white centers found on the mucosal surface of the oral cavity

Clinical Presentation

- Exanthem Phase
  - Initial appearance of discrete macules and papules on scalp, forehead, and behind ears
  - Spreads to torso and extremities over ensuing 2-3 days
  - Lesions become confluent and eventually fade in order of anatomic appearance over the next several days
    - Fades to brown or copper color

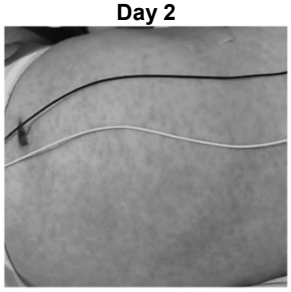
Exanthem Phase



CDC Public Health Image Library

Exanthem Phase

Day 2



Day 5

Complications

- Complications are common, especially in young children
- Most frequent complications:
  - Acute otitis media
  - Diarrhea
  - Febrile seizures
- Common severe complications:
  - Dehydration
  - Bronchopneumonia
  - Laryngotracheobronchitis

Neurological Complications

- Post-infectious encephalomyelitis (1 in 1000 cases)
  - Highest occurrence in adolescents and adults
  - Abrupt recurrence of fevers 3-10 days after rash onset
    - Seizures, altered mentation, focal neurological signs
  - Due to aberrant immune response – no virus in CNS
- Subacute sclerosing panencephalitis (1 in 10-100k cases)
  - Persistence of virus in CNS for years
  - Slowly progressive infection with multifocal demyelination
  - Subtle symptoms ultimately progress to vegetative state / death

Other Complications

- Pneumomediastinum
- Mediastinal emphysema
- Hepatitis
- Appendicitis
- Keratitis
- Myocarditis
- Pericarditis
- DIC

Immunocompromised Hosts

- May have altered presentation of disease
  - "classic measles" followed by reappearance of rash
  - Non-specific illness without rash
- Diffuse progressive pneumonitis is leading cause of death
- Measles inclusion body encephalitis may occur in patients with T-cell immunodeficiency
  - Progressive CNS infection 1-6 months after acute infection
  - Mental status changes and seizures in absence of fevers
  - Very high mortality

Diagnosis and Management

Diagnosis

- Testing coordinated through public health
- RT-PCR
  - Sensitivity depends on specimen collection and timing
    - Nasopharyngeal and oropharyngeal specimens have greater sensitivity relative to urine specimens
    - Highest sensitivity if collected within 3 days of rash onset
- Serology
  - IgM positive when rash appears in 60-70% of cases
    - May be detectable for up to 1 month after rash onset

Test Interpretation

- RT-PCR
  - Positive result confirms presence of measles virus
    - Patients recently immunized with MMR may test positive via PCR for up to 1-month post-vaccination
    - Genotyping is used to distinguish vaccine strain from wild-type
  - Negative result supports but does not confirm absence of virus
    - False negatives may occur if specimen collected late after rash onset or with improperly collected or stored specimen

Test Interpretation

- Serology
  - Interpretation impacted by pre-test probability of disease
  - Positive IgM supports but does not prove infection
    - False positives may occur with other viral illnesses
    - May also be positive in weeks after MMR vaccination
  - Negative IgM may occur in samples collected early in illness
    - Convalescent serologies may retrospectively confirm or disprove infection

Management

- Supportive care directed at symptom relief
- Early recognition of secondary bacterial infections
- Education to families:
  - Return precautions
  - Emphasis on maintaining hydration for young children
  - Home isolation
- Vitamin A
  - Recommended for all children with measles, regardless of country of residence

Measles Prevention

MMR Vaccination

- Attenuated live-viral vaccine
  - Contraindicated in pregnant or immunocompromised patients
- Very high vaccine effectiveness
  - 93 to 95% effectiveness after 1 dose, 97 to 99% after 2 doses
- Two-dose series recommended for children
  - Dose 1 at 12-15 months of age, dose 2 between 4-6 years
  - Early Dose 0 may be given as young as 6 months of age
    - Prior to international travel
    - Domestic travel or residence in areas experiencing outbreak

MMR Vaccination

- Adult vaccination recommendations
  - Born 1957 to 1967 – may have received inactivated vaccine
  - Born 1968 or later – verify receipt of MMR
- Which adults need 2 doses of MMR?
  - Healthcare workers
  - Students at post-high school educational institutions
  - Prior to international travel
  - People with HIV infection
  - Household and close contacts of immunocompromised

Vaccine Myths

- Natural immunity is preferred
  - Misperception of severity of measles infection & complications
- MMR causes autism
  - Fraudulent study investigating 12 children in 1998
  - Numerous extensive studies involving hundreds of thousands of children have subsequently disproven this myth
- MMR contains thimerosal, aluminum, or mercury
- Recently vaccinated people are contagious to others
  - Live virus is not shed and cannot be transmitted to others

Post-Exposure Prophylaxis

- MMR vaccine
  - Exposed persons 6 months of age and older who have received less than 2 doses of MMR
  - Must administer within 72 hours if no prior MMR doses
- Immune globulin
  - Administer within 6 days of exposure to individuals at risk of severe illness who cannot receive MMR
    - Intramuscular IG: young infants
    - Intravenous IG: immunocompromised and pregnant

Preventing Healthcare Transmission

- Healthcare settings represent an important area of secondary measles transmission
  - Transmission during the prodromal phase is particularly challenging due to non-specific clinical presentation
- Ensure all healthcare staff have evidence of immunity
  - 2 documented doses of MMR, or
  - Laboratory evidence of immunity (i.e., positive IgG)
  - Birth before 1957 should not be used as presumptive evidence of immunity in an outbreak setting

Preventing Healthcare Transmission

- Rapid identification of suspected cases
  - Electronic medical record alerts
    - International travel
    - Symptoms
    - Vaccine status
  - Visual alerts and signs for patients & visitors
  - Ready access to masking & PPE
  - Frontline clinician education on signs & symptoms of measles

If you think your child may be sick due to a measles exposure, please tell a staff member right away.

Ensure signage is translated into multiple languages to match patient population

Preventing Healthcare Transmission

- Rapid isolation of suspected cases
  - Immediately place in Airborne Infection Isolation Room (AIIR)
  - Only staff with evidence of immunity should enter
  - Adhere to Standard and Airborne Precautions
  - If no AIIR available, place in private room with door shut
- Identify potentially exposed patients, staff, and visitors
  - In shared air space with infectious patient at the same time (without PPE), or vacated within the prior 2 hours
    - Time frame may be shorter dependent upon ventilation

Common Clinical Questions

Vaccine Reaction or Infection?

- Common MMR reactions include fever (10%) and rash (5%)
- May be challenging due to overlapping clinical features:

	Vaccine Reaction	Wild-Type Measles
Fever	May be Present *Tmax up to 38.5C to 39C*	Present *Tmax up to +40C*
Three "C's"	Absent *Unless concurrent viral URI*	Present *Note: Conjunctivitis may be absent*
Known Exposure or Travel History	Absent	Present *May be absent during local outbreak*
Positive PCR Test	May be Present *Distinguishable by Genotyping*	Present

Vaccine Reaction or Infection?

- Key distinguishing features suggestive of vaccine reaction:
  - (Lack of) exposure history will serve as primary guide
  - Timing post-immunization (usually 1-2 weeks post-MMR)
  - Absence of respiratory symptoms
  - Rash occurring prior to fever onset also suggests reaction

When to administer MMR dose 0?

- An early dose of MMR (i.e., dose 0) may be administered to infants as young as 6 months of age
- Recommended to administer in the following scenarios:
  - Ahead of international travel to any country outside the U.S.
  - Residence or travel domestically to any county within the U.S. in which local public health officials recommend dose 0 vaccination
    - Not every U.S. county with an active outbreak will have this recommendation
    - Check current state and local public health guidance

Immune Blunting due to Dose 0

- Termed 'dose 0' as early immunization does not replace need for two doses beginning at 12 months of age
  - Higher rate of primary vaccine failure at younger ages
  - Pooled VE estimate of 58% when administered at 6-9 months
- Early MMR administration is associated with accelerated decline in measles-specific neutralizing antibodies
  - Most pronounced when administered **< 9 months** of age
  - Subsequent dosing does not appear to correct this decline
  - Durable T-cell response still suggests strong protection

Can MMRV be used as an early dose 2?

- An early 2nd dose of measles-containing vaccine before 4 to 6 years of age is recommended:
  - Ahead of international travel
  - In outbreak areas as recommended by public health
- MMR dose 2 may be administered as soon as 28 days following MMR dose 1
- MMRV may be administered early, with a recommended interval of 3 months between vaccine doses
  - No negative impact to varicella vaccine effectiveness

Summary

Summary

- Measles virus is highly contagious – droplets & aerosols
- Respiratory illness with fever, rash, and three “C’s”
  - Not a subtle infection
  - Prodrome may be indistinguishable from other viruses
  - Use risk factors to guide assessment: travel, exposures, vaccines
  - Complications are common
- Notify public health with any suspected cases
- Maintain readiness and most importantly, encourage MMR