The Resurgence of Affliction
Measles: The Current Situation

New Jersey Immunization Network
Webinar
June 2, 2011
Global Situation*

- In 2008, ~83% of the world’s children received one dose of measles-containing vaccine (MCV) by their first birthday
  - Up from 72% in 2000
- In 2008 there were an estimated 164,000 deaths due to measles
  - A 78% decrease (733,000 deaths) since 2000
  - >95% of deaths in low-income countries with weak health infrastructures
  - Mainly seen in children <5 years of age
- All regions, except one (South-East Asia), have achieved a 90% reduction in measles mortality from 2000-2010
  - Two years ahead of UN goals
  - South-East Asia experienced a 46% decrease in measles mortality
    - Delayed implementation of large scale vaccination campaign in India
      - 75% of measles mortality in children in India
- In jeopardy due to decreased financial and political commitment
  - Estimated 1.7 million measles-associated deaths between 2010-13

*WHO estimates. See http://www.who.int
Measles global annual reported cases and MCV coverage, 1980-2009

Source: WHO/IVB database, 2010
93 WHO Member States. Data as of September 2010

Date of slide: 08 September 2010
United States

- **Prevaccine era (pre-1963)**
  - ~500,000 cases annually
  - In reality, ~4 million infected/year
    - ~500 deaths
    - ~150,000 with respiratory complications
    - ~48,000 hospitalizations
    - 7,000 seizure episodes
    - 4,000 cases of encephalitis
    - Up to 25% of people with measles-associated encephalitis were permanently brain damaged or deaf
United States (continued)

- Since 1963 (vaccine licensure)
  - 99% decrease in measles incidence
    - Most pronounced decrease seen with enactment of laws requiring vaccination for school entry in early 1980’s
  - From 1985 – 1992
    - Children with exemptions were 35x more likely to contract measles than nonexempt children*

- 1989-1991 resurgence
  - Estimated 55,000 measles cases with >130 deaths
  - Controlled by:
    - Increased rate of immunization
    - Institution of 2-dose regimen in children

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United States (continued)

- Measles elimination (i.e., interruption of endemic measles transmission) was declared in the US in 2000
- Median of 56 cases from 2001 – 2008*
  - Range: 37 - 140
  - Associated with imported infection
- January – May 20, 2011*
  - 118 cases reported from 23 states and New York City
    - More than reported for 2010
    - Highest number reported for this period since 1996

Measles (Rubeola)

Virology

- Genus: *Morbillivirus*
- Family: Paramyxoviridae
- Canine distemper and rinderpest viruses
- Spherical, enveloped, single-stranded RNA virus
  - 6 identified structural proteins
    - 3 complexed with RNA to form nucleocapsid P, L, and N proteins
    - 3 complexed with viral envelope (F, H, and M proteins)

http://biowiki.org/twiki/pub/Fall09/MeaslesVirus/Measles_virus.JPG
Measles
Virology

Genetic variety

- WHO recognizes 23 genotypes
  - phylogenetic analysis of the N gene
- Biologic significance unknown
- Allows monitoring transmission pathways
- Immune response generated through immunization protects vs all strains
  - Molecular sequencing can distinguish between wild-type and vaccine-virus
Measles
Pathophysiology

- Infects epithelial, reticuloendothelial, and white blood cells
  - Multiple organ systems
    - Multinucleated giant cells found throughout the respiratory and GI tracts and in most lymphoid tissue on autopsy
  - Decline in CD4 cells
    - Prior to rash onset and lasting up to 1 month
      - Suppression of delayed-type hypersensitivity

Perry RT, Halsey NA. The clinical significance of measles: a review. JID. 189 (Suppl 1) S4-S16. May 1, 2004
Measles
Epidemiology

- Humans are the only natural hosts
  - No animal reservoirs

- Highly contagious
  - Attack rate in susceptible household contacts: 75%-90%
  - Direct contact with infectious respiratory secretions
    - Large respiratory droplets and droplet nuclei
      - Lingers for at least 2 hours
      - Requires airborne precautions
    - Nasopharynx and conjunctiva
    - Most infectious in prodromal period
      - Before rash onset
Measles
Epidemiology

- Incubation period: 8-12 days
- Contagious period: 1-2 days before symptom onset (3-5 days before rash) to 4 days after rash appearance
  - Immunocompromised patients may demonstrate prolonged excretion of virus
- Peak incidence in temperate regions is late winter and spring
- Pre-vaccine era
  - Pre-school and young school age children
  - Few susceptibles by 20 years of age
- Primary vaccine failure (≥12 months) ~5%
  - Most infections in previously immunized children viewed as primary vaccine failures
Measles
Clinical Presentation

- **Prodrome (2-4 days)**
  - Fever (39°C–40.5°C), cough, coryza, and conjunctivitis
    - Symptoms intensify and usually peak on first day of rash
  - Appearance of Koplik spots appear 1 day prior to rash onset and last 2-3 days
    - Buccal mucosa opposite 1st molar
    - Soft palate, conjunctiva, vaginal mucosa

Perry RT, Halsey NA. The clinical significance of measles: a review. JID. 189 (Suppl 1) S4-S16. May 1, 2004
Koplik Spots

http://www.pathguy.com/sol/24924.jpg
Measles
Clinical Presentation

- Rash first appears on face and neck
  - Discrete erythematous patches (3-8 mm)
- Lesions increase and spread downwards to trunk and extremities (including palms in 25%-50%)
  - Most intense over face and trunk
    - Frequently become confluent
- Rash persists for 3-7 days
  - Desquamation may appear but not pronounced
  - Severe desquamation seen in malnourished children
- Immunocompromised patients may demonstrate an atypical presentation
  - Without rash

Perry RT, Halsey NA. The clinical significance of measles: a review. JID. 189 (Suppl 1) S4-S16. May 1, 2004
Measles
Clinical Presentation

- Common associated signs and symptoms
  - Photophobia secondary to iridocyclitis
  - Sore throat
  - Headache
  - Abdominal pain
  - Generalized mild lymphadenopathy
Measles Complications

- **At greatest risk**
  - <5 years and ≥20 years
  - Immunocompromised
    - T-cell suppression
      - Congenital or acquired T-cell deficiencies
        - 60% of all measles-associated deaths in NJ in 1990-1991 occurred in HIV-infected children*
      - Chemotherapy for cancer or steroid therapy
      - Bone marrow transplantation
  - Malnourished
    - Protein losing enteropathy, increased metabolic demand, decreased food intake
    - Vitamin A deficiencies
      - Measles infection lowers serum retinol levels
  - Crowded living conditions
    - Developing countries

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Measles
Complications-Respiratory

- **Pneumonia**
  - Most common severe complication
    - Responsible for most measles-associated deaths
  - Viral
    - Measles
    - Secondary infection with adenovirus or HSV
  - Bacterial
    - *Streptococcus pneumoniae, Staphylococcus aureus, Haemophilus influenzae* and others
  - Immunocompromised patients
    - Diffuse progressive pneumonitis
      - Most common cause of death
    - Hecht’s giant cell pneumonia

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Measles
Complications-Respiratory

- **Otitis media**
  - Most common complication reported in US
    - 14% of children under 5 years of age

- **Laryngotracheobronchitis**
  - “measles croup”
  - 9%-32% of US children hospitalized with measles
    - 2nd most common cause of death in hospitalized US children after pneumonia
  - Secondary bacterial tracheitis, pneumonia or both
    - *S. aureus* most commonly cultured organism
Measles Complications - Neurological

- **Febrile seizures**
  - 0.3%-2.3% in children in US and UK
  - Benign, not associated with residual damage

- **Encephalitis**
  - Postinfectious encephalomyelitis (PIE)
    - 1-3/1000 infections
    - 3-10 days post rash onset
    - Highest incidence in adolescents and adults
    - ~25% case fatality rate
    - ~33% have neurological sequelae
  - Subacute sclerosing panencephalitis (SSPE)
    - Persistence of measles virus in CNS
    - Slowly progressive infection and demyelination
      - Vegetative state
      - 7-10 years post acute infection
    - 1/8.5 million cases in the US
      - Disappeared sin the US since advent of measles immunization

- **Measles inclusion body encephalitis**
  - Immunocompromised
  - Mental status changes and seizures without fever

Perry RT, Halsey NA. The clinical significance of measles: a review. JID. 189 (Suppl 1) S4-S16. May 1, 2004
Measles
Complications-GI and Ocular

**Diarrhea**
- Most common in people <5 years and >30 years
- 30%-70% of hospitalized patients with measles in US
- Typical onset just before rash
- Dehydration common

**Blindness**
- Keratitis (inflammation of the cornea)
  - Common
  - Secondary infections with viruses (adenovirus, HSV) and bacteria (*Pseudomonas* spp. and staph)
  - Scarring and blindness
- Vitamin A deficiency
- Cortical damage secondary to encephalitis

Perry RT, Halsey NA. The clinical significance of measles: a review. JID. 189 (Suppl 1) S4-S16. May 1, 2004
Measles Diagnosis

- **Serology**
  - Positive IgM for measles
    - Collect serum at first encounter with suspected measles patient
    - *30% false negatives when collected within 72 hours of rash onset*
      - Confirm with second sample collected ≥72 hours of rash onset
      - If negative and high index of suspicion remains repeat IgM study
  - Paired acute and convalescent IgG studies
    - Not appropriate for timely diagnosis
  - Serology may be difficult to interpret in those previously vaccinated or who received PEP vaccination or immunoglobulin
Measles Diagnosis

- **Isolation of measles virus**
  - Collect samples as soon as possible after rash onset
    - Isolation most successful if specimen collected from day of rash onset through 3 days post-onset
  - Throat or nasopharyngeal swabs preferred
    - Virus isolation or RT-PCR detection
    - Flocked synthetic swabs (dacron) preferred
      - Do not use cotton
        - Contain substances that inhibit enzymes in RT-PCR
        - Avoid wooden and calcium alginate swabs
    - Place swabs in 2 mL of standard commercially available viral transport media (VTM)
      - Cell culture medium can be used
      - If VTM not available use sterile isotonic solution (e.g., phosphate buffered saline)
        - Place swab in 1-3 mL in a sterile container
        - Blood collection tube with no gels/other agents or sterile urine collection container
      - Place specimen in refrigerator until transport
  - Urine sample
  - Sensitivity increased if both are sent
Measles
Treatment

- Supportive care
- No antiviral treatment
  - No controlled clinical trials evaluating ribavirin
    - Not FDA approved for treatment of measles
- Appropriate antimicrobials for secondary bacterial infections
- Vitamin A therapy
  - Developing countries
    - Therapy associated with decreased morbidity and mortality
  - United States
    - Low serum Vitamin A levels in children
    - Severe measles associated with lower Vitamin A serum concentrations
  - WHO recommends Vitamin A therapy for all children with measles regardless of country
    - Once daily for 2 days
    - 200,000 IU for children ≥12 months
    - 100,000 IU for children 6 through 11 months
    - 50,000 IU for children <6 months
Measles
Prevention-Immunization of Children

- **Two dose schedule**
  - All children
    - First dose: 12-15 months of age
    - Second dose: 4-6 years of age
    - May get 2nd dose ≥28 days after 1st dose
  - **If traveling abroad**
    - 6-12 months of age, prior to travel
    - Then follow standard schedule (see above)
Measles
Prevention-Immunization of Adults

- All adults should have proof of immunity
  - Born in US before 1957
    - Exceptions
      - Health care personnel
        - If no serologic evidence of immunity then MMR x 2
        - Interval ≥28 days
  - Serologic proof of immunity
  - Documented receipt of measles-containing vaccine
    - Two doses at appropriate age and interval
  - Physician-diagnosed disease is not acceptable
Measles
Prevention-Post Exposure Prophylaxis (PEP)

- Intramuscular immune globulin (IG) can be given up to 6 days post-exposure
  - Delay giving children MMR 5-6 months after receiving IG depending on the dose

- IVIG preparations usually contain adequate amount of measles antibodies
  - For those receiving IVIG regularly, 400mg/kg should be adequate for prophylaxis for exposures occurring within 3 weeks of receiving IVIG
The Situation
WHO’s European Region 2011

- As of May 6, 2011
  - 38 countries
  - 7028 confirmed cases of measles
    - 2632 (37%) are laboratory-confirmed
    - 3929 (60%) are clinically confirmed
    - 467 (3%) are epidemiologically confirmed
  - 29% of cases in people who never received a measles-containing vaccine (MCV)
  - 67% of cases in people who had no documentation or did not know their vaccination status
Age Distribution of Measles Cases Reported in 2011 in the WHO European Region (N=7028)

WHO Epidemiological Brief. No, 14. May 2011
Measles Incidence in 2010 and Outbreaks Between January 2010 and March 2011, WHO European Region

France: ~10,000 cases in first 4 months of 2011
360 cases of severe measles pneumonia
12 cases of encephalitis
6 measles related deaths
Number of Measles Cases per Month, Mandatory Notification
France, January 2008 – March 2011

http://www.invs.sante.fr/surveillance/rougeole/Point-rougeole_190411.pdf
The Situation
United States

- January – May 20, 2011
  - 118 cases reported in 23 states and New York City
    - 105/118 (89%) were associated with importation
      - 46/105 (44%) importations
        - 34/46 (74%) among US residents traveling abroad
        - 12 (26%) among foreign visitors
        - 40/46 (87%) were from the WHO European and South-East Asia regions
    - 47/118 (40%) were hospitalized
      - 9/47 (19%) had pneumonia
    - 105/118 (89%) were laboratory-confirmed
      - 52/105 (50%) measles virus RNA detected

Age distribution

- Range: 3 months to 68 years
  - 18 (15%) were <12 months
  - 24 (20%) were aged 1-4 years
  - 23 (19%) were 5-19 years
  - 53 (45%) were ≥20 years

The Situation
United States

Vaccination status

- 105/118 (89%) were unvaccinated
  - 39/45 (87%) of US residents aged 12 mos–19 years
    - 24/39 (62%) had a religious or personal exemption
    - 8/39 (21%) missed opportunity for vaccination
  - 35/42 (83%) of US residents aged ≥20 years
    - 6/35 (17%) declined vaccination due to philosophical objections
  - 30/33 (91%) of US residents who traveled and were vaccine-eligible
    - 1/33 (3%) received 1 of the 2 recommended doses

Three confirmed and one probable case

- Two confirmed cases are secondary to exposure to imported cases
  - France, Italy
- 21 month-old from Middlesex county
  - Unvaccinated
  - Travel to Pakistan

Since 2005

- Range confirmed and probable cases: 1-3/year

April 13 – May 13, 2011

- 12 exposure/case investigations
  - Involving hundreds of exposures

Personal communication. Vaccine Preventable Diseases Division, NJDHSS
Two lab-confirmed (IgM +) cases

- Presented with fever and rash on 4/12-13
  - Morris County ED
- Arrived via Newark Liberty Airport on 4/7
- Transmission to unvaccinated 8 month old
  - Dates of exposure: 4/7 – 4/13
  - Quarantine at home beginning 4/13
    - Both parents had serologic proof of immunity
    - Received PEP 6 days post-exposure
  - Developed rash on 4/18

Personal communication. Vaccine Preventable Diseases Division, NJDHSS
The French Connection
New Jersey, April 7 – May 12, 2011

Contact follow-up
- On flight to NJ
  - 16 passengers
- Hospital contacts from 4/12-13
  - >15 patients
  - >7 staff
- Family exposure
  - Two families
    - 7 people
    - 3 unvaccinated children (2/3 ≤12 mos)
- Restaurant exposure (family get-together)
  - Unknown number (>20 people)
    - Other patrons (unknown)
    - Press release to notify patrons
- Staff
  - ~5 people

Personal communication. Vaccine Preventable Diseases Division, NJDHSS
Milan to Rhode Island to New Jersey  
April 12 – May 13, 2011

- Index case arrived at JFK on 4/12
  - Three NJ residents exposed on flight
- An additional NJ resident exposed on index case arrival
  - Colleague of index case
  - Received MMR as PEP within 24 hours of exposure (4/13)
    - Reported had received MCV in past but no documentation
  - RI DOH notified NJDHSS that contact was symptomatic on 4/25
    - Traveled extensively while infectious within and outside of NJ

Personal communication. Vaccine Preventable Diseases Division, NJDHSS
Contact follow-up

- Secondary case
  - Involved multiple jurisdictions in multiple states
  - Immediate family (3)
  - Family/friends/nanny includes Easter dinner in home (~18)
  - Passengers on multiple flights (~286)
  - Clients (~4)
  - Businesses contacts (~400)
Health Care-Associated Measles Outbreak
Tucson, Arizona, 2008*

- Infected visitor from Switzerland
  - 14 patients with confirmed measles
    - All unvaccinated or unknown status
    - 11 patients accessed health care services while infectious
    - Transmission to 7 patients in a health care facility
    - 1 patient was promptly masked and isolated upon rash onset
  - Health care personnel (HCP) immunity data from 2 hospitals
    - 1776/7195 (25%) lacked evidence of measles immunity
      - 139/1583 (9%) HCPs tested seronegative
    - No computerized HCP employee medical records
  - Cost in 2 hospitals: $799,136.00

The Dilemma

- Measles remains endemic in many parts of the world
  - The world is a village
- Measles is highly contagious
  - Airborne transmission
  - Most contagious prior to presentation of rash
    - Resembles upper respiratory tract infection
- Low index of suspicion in regions where control has been most successful
  - Diagnosis and institution of infection control interventions commonly delayed
- On reintroduction into regions of low endemicity or where elimination has been achieved
  - Serious consequences of disease especially in vulnerable populations
  - Great expense in time and money to public health and medical entities as well as to society as a whole
NJDHSS Recommendations

- Review immunization status of all patients
  - Review status of those with medical or religious exemptions
  - Offer vaccine if appropriate
- Review immunization status of all staff
  - Meet current criteria for proof of immunity
- High index of suspicion
  - Awareness of current situation
  - Careful consideration of patient history
    - Travel history (awareness of outbreaks globally)
    - Exposure history
    - Immunity
NJDHSS Recommendations

- Rigorous adherence to appropriate recommended infection control interventions
  - On suspicion of measles
    - Immediate isolation with airborne precautions in a negative pressure room
    - If hospitalized, remain in airborne isolation through day 4 of rash onset
    - Room used by suspected measles-infected patient should not be used for 2 hours after patient leaves
  - Measles exposure
    - Quarantine from day 5 from first exposure to day 21 after last exposure
  - In general
    - Appropriate triage for patients with respiratory tract symptomology and febrile rashes
    - Surgical masks for coughing patients, particulate respirators for exposed HCP
NJDHSS Recommendations

- Immediate notification of appropriate public health authorities upon suspicion of measles
  - Local Health Department of patient’s residence
  - [http://www.state.nj.us/health/lh/index.shtml](http://www.state.nj.us/health/lh/index.shtml)
  - If unable to reach the local health department contact:
    - NJDHSS at **609-826-5964** (regular business hours)
    - Vaccine Preventable Disease Service at **609-826-4861**
    - **609-392-2020** (holidays/off hours)

- Continued support for measles elimination (and hopefully eventual eradication) programs globally
Resources

- Journal of Infectious Diseases, Volume 189, Supplement 1, May 1, 2004
  - http://jid.oxfordjournals.org/content/189/Supplement_1.toc


- NJDHSS-Vaccine Preventable Disease Program
  - http://www.state.nj.us/health/cd/vpdp/index.shtml

- CDC.
  - http://www.cdc.gov

- WHO.
  - http://www.who.int
Thank You

Questions??

Email:

NewJerseyImmunizationNetwork
@njpcore.org