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 goal
  - South-East Asia experienced a 46% decrease in measles mortality
  - Declined 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
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
    - 4,900 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


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)

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

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

- 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

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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

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

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

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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

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

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Measles Complications-Neurological

- Febrile seizures
  - 0.2%-2.3% in children in US and UK
  - Benign, not associated with residual damage
- Encephalitis
  - Postinfectious encephalomyelitis (PIE)
    - 1-3/1000 infections
    - More common post scarlet fever
    - Greatest incidence in adolescents and adults
    - <=2% 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 from acute infection
      - 1/10,000-15,000 cases in the US
      - Disappeared in 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

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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

- **Isolation of measles virus**
  - Collect swabs as soon as possible after rash onset
    - Isolation most successful if specimens collected from day of rash onset through day 4 post onset
  - Throat or nasopharyngeal swabs preferred
  - Flocked synthetic swabs (dacron) preferred
    - Do not use cotton swabs
    - Contain substances that inhibit enzymes in RT-PCR
    - Avoid wooden and calcium alginate swabs
  - Place in 2 mL of standard commercially available viral transport media (VTM)
    - Cell culture medium can be used
  - If VTM not available use sterile saline solution (e.g., phosphate-buffered saline)
    - Dilute specimen 1:10 in saline
    - Resuspend swab residue in saline
  - Place in refrigerator until transport
  - Sensitivity increased if both are sent

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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 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 (99%) were laboratory-confirmed
    - 52/115 (45%) measles virus RNA detected

**The Situation**  
**United States**

- **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


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**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


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**The Garden State**  
**January – May 27, 2011**

- 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

*Personal communication. Vaccine Preventable Diseases Division, NJDHSS*
The French Connection
New Jersey, January – May 13, 2011

- 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
    - >35 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
Personal communication. Vaccine Preventable Diseases Division, NJDHSS

Milan to Rhode Island to New Jersey
April 12 – May 13, 2011

- 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
- Travel history (awareness of outbreaks globally)
- Exposure history
- 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
- 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
  - If unable to reach the local health department contact:
    - NJDHSS at 609-826-5964 (regular business hours)
    - Vaccine Preventable Disease Service at 609-826-4061
    - 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??

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