

# MEASLES in 2011



## CLINICIAN EDUCATION SLIDES

Infectious Disease Department  
Infection Prevention and Control Department

Medical Education Department

**Children's Hospitals and Clinics of Minnesota**

**Posted 3/30/11**



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# What's in a Name?

- **Rubeola:**
- **English Measles**
- **Hard measles**
- **Red measles**
- **7-day measles**
- **Rubella:**
- **German measles**
- **3-day measles**



# The Paramyxoviridae Family



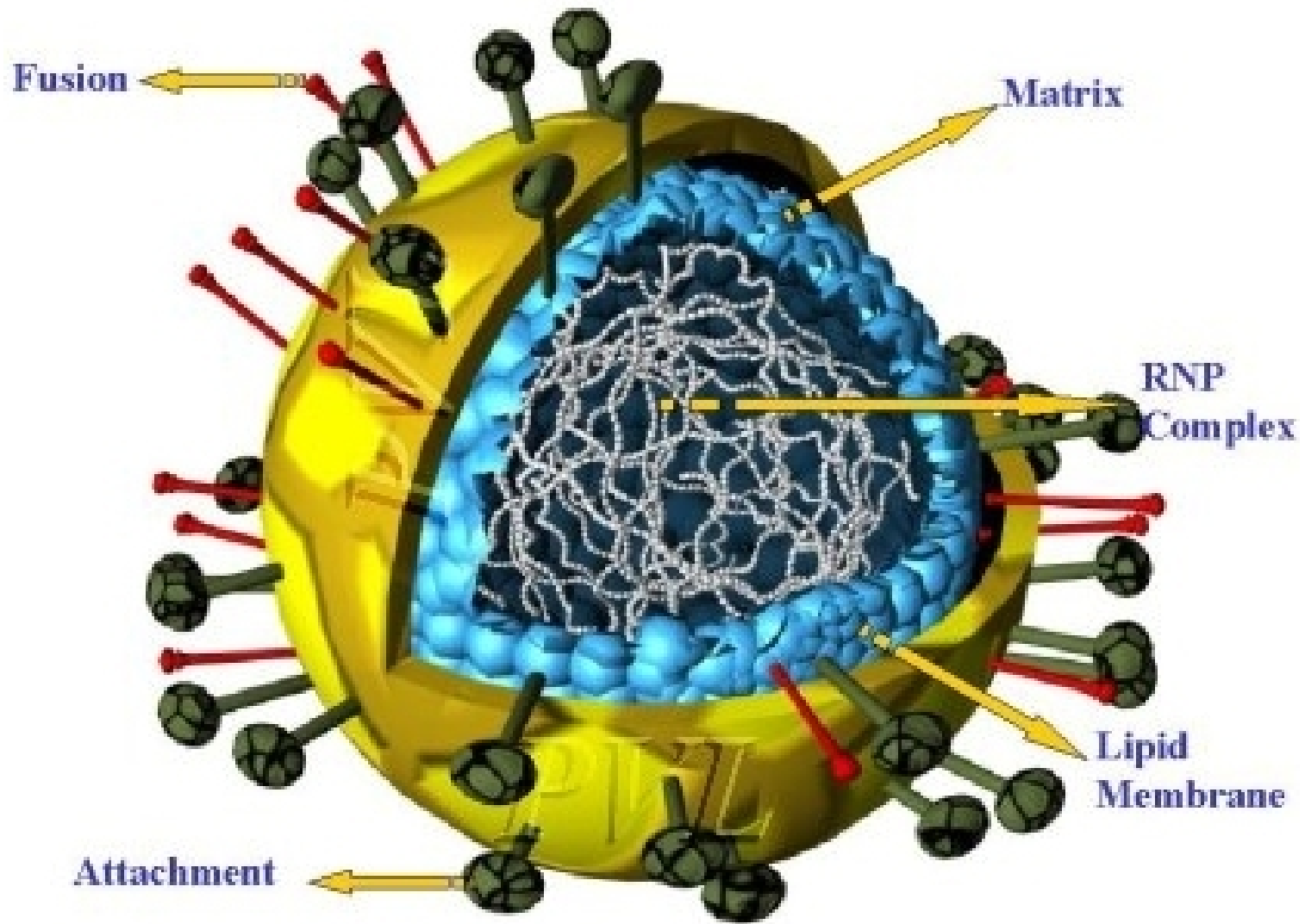
## I. Paramyxovirinae

- A. Paramyxovirus – parainfluenza 1,3
- B. Rubulavirus – parainfluenza 2, 4a, 4b, mumps
- C. Morbillivirus – **MEASLES**  
    (“morbilliform rash”)

## II. Pneumovirinae

Respiratory syncytial virus





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# Key Points – Paramyxoviridae Biology

- The entire family of viruses has high affinity for respiratory epithelium
- The entire family has *less genetic variability and structural complexity than influenza* (orthomyxovirus)
- Measles and mumps extend beyond the respiratory tract
- Parainfluenza, RSV do not generally extend beyond the respiratory tract



# Core Clinical Features of Measles

- Prodrome may last several days, resembles other viral illnesses
- Measles is heralded by **FEVER** (often high)
- The three C's emerge:
  - CONJUNCTIVITIS** (watery, usually non-purulent)
  - CORYZA** ( rhinitis)
  - COUGH** (non-specific, “croupy cough” sometimes described)
- **KOPLIK'S SPOTS** (appear transiently)
- Then **RASH** emerges and may last a week or more



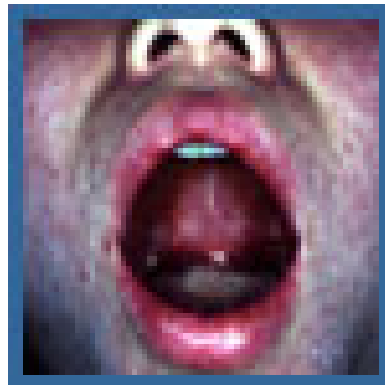
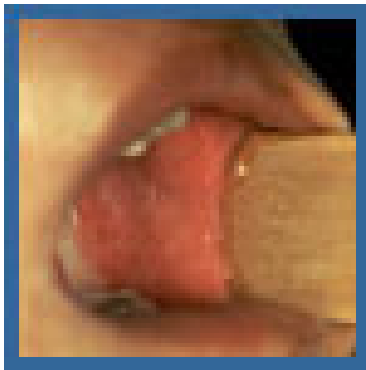
# Koplik Spots



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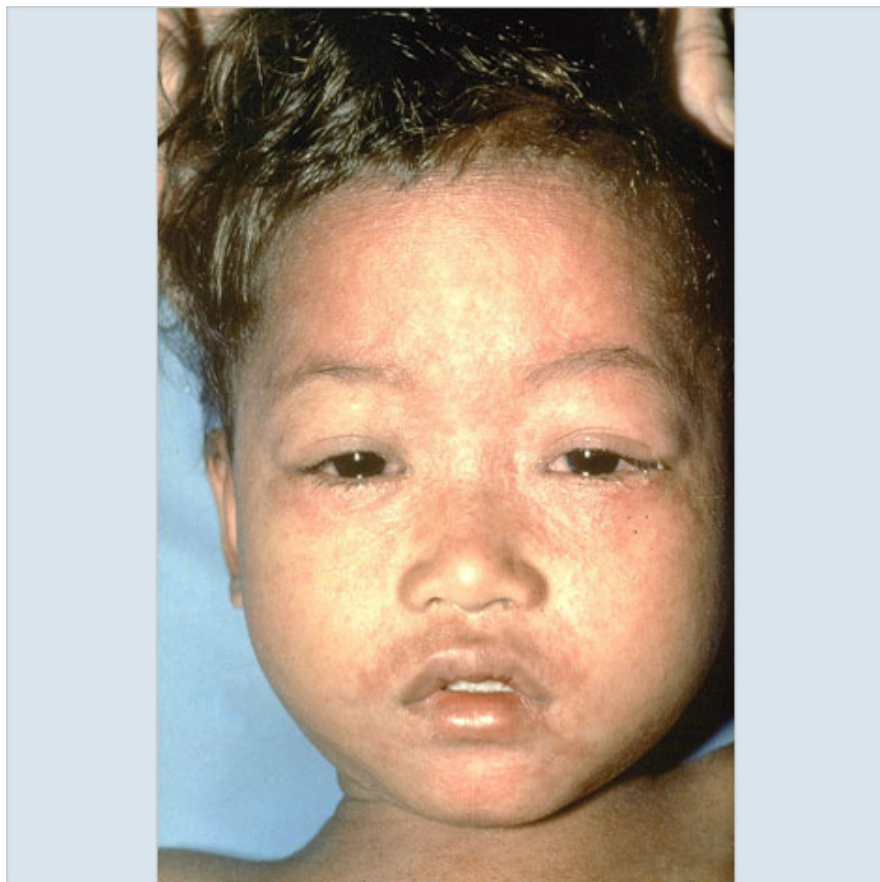
# Koplik Spots

- If you are lucky at this early point (1-2 days before rash) you will see Koplik spots, which are present only a few days.
- Looks like coarse salt sprinkled over the buccal mucosae that doesn't last long.
- It is diagnostic of measles if you see it.





# Characteristic Measles Rash



- Maculopapular, starts on hairline, then spreads across face to trunk “like a bucket of virus poured over the head”
- Lasts 4-6 days or longer
- Clears in the same order
- One is most contagious 4 days before and 4 days after rash onset.



# Clinical Features Reflect Measles Pathogenesis

- **Virus arrives at upper respiratory tract – contact/aerosol – cell receptors**
- **Local replication, then dissemination via lymphoid system -- primary viremia**
- **Multi-organ infection, viral replication, then secondary viremia**
- **Mucosal, skin features appear, viremia usually ends, urine virus shedding continues**



# General Histology of Measles

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- **MULTINUCLEATED GIANT CELLS** are a key finding in reticuloendothelial cells, resp. epithelium (Warthin-Finkeldy cells)
- **Skin and mucosal lesions (Koplik's spots)** have similar histology, perivascular infiltrates but no giant cells
- **“Giant cell pneumonia”** is primary measles pneumonia



# Critical Organ Involvement in Measles

- **PULMONARY INFECTION**

- Primary measles pneumonia
- Secondary bacterial pneumonia

- **CENTRAL NERVOUS SYSTEM INFECTION**

- Acute encephalitis during measles – (1/1000 cases)
- Subacute sclerosing panencephalitis (delayed by years, 1/100,000 to 1/1,000,000) – progressive and fatal\*



# Measles and Immunity

- **IMPORTANCE OF ANTIBODY –**
  - Transient IgM response, then IgG
  - Best correlate of immunity is anti-H IgG
  - SSPE patients have lack of anti-M IgG
  
- **IMPORTANCE OF CELLULAR IMMUNITY**
  - Appears important in recovery from measles
  - Agammaglobulinemic patients do well w/ measles
  - May be important in lifelong immunity



# Passive and Active Immunity



- Immunity to measles may be brought about by **active** administration of antigen (vaccine) or by **passive** administration of antibody
- In contrast with strategies for other pathogens (hepatitis B, rabies, etc.), a strategy using combined active/passive immunity is not possible for measles



# Pre-Vaccine Era Epidemiology



- **A universal infection of children**
- **Millions of measles deaths occurred annually in the world, greater in developing countries, especially in the undernourished**
- **Annual USA cases in hundreds of thousands, hundreds of deaths, cycling in waves every 2-3 years, some seasonality (Jan→Apr), never entirely absent.**



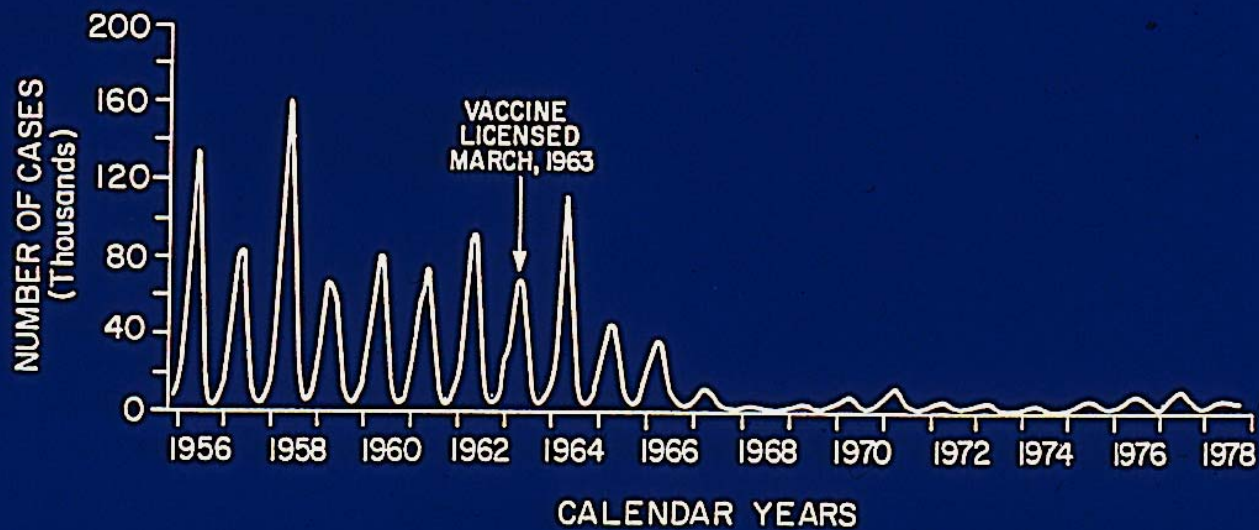
# Measles Vaccine: 1963-1967

- **Recapitulation of polio vaccine debate, i.e. killed vs. live virus**
- **Attempts to attenuate vaccine reactions by the simultaneous use of gamma globulin**
- **Evidence of superiority of live vaccine emerged, dissatisfaction with IMIG**
- **Completion of mumps and rubella vaccine 1967-1969 and incorporation into M.M.R. vaccine**





REPORTED CASES OF MEASLES BY FOUR WEEK PERIODS  
UNITED STATES 1956-1978



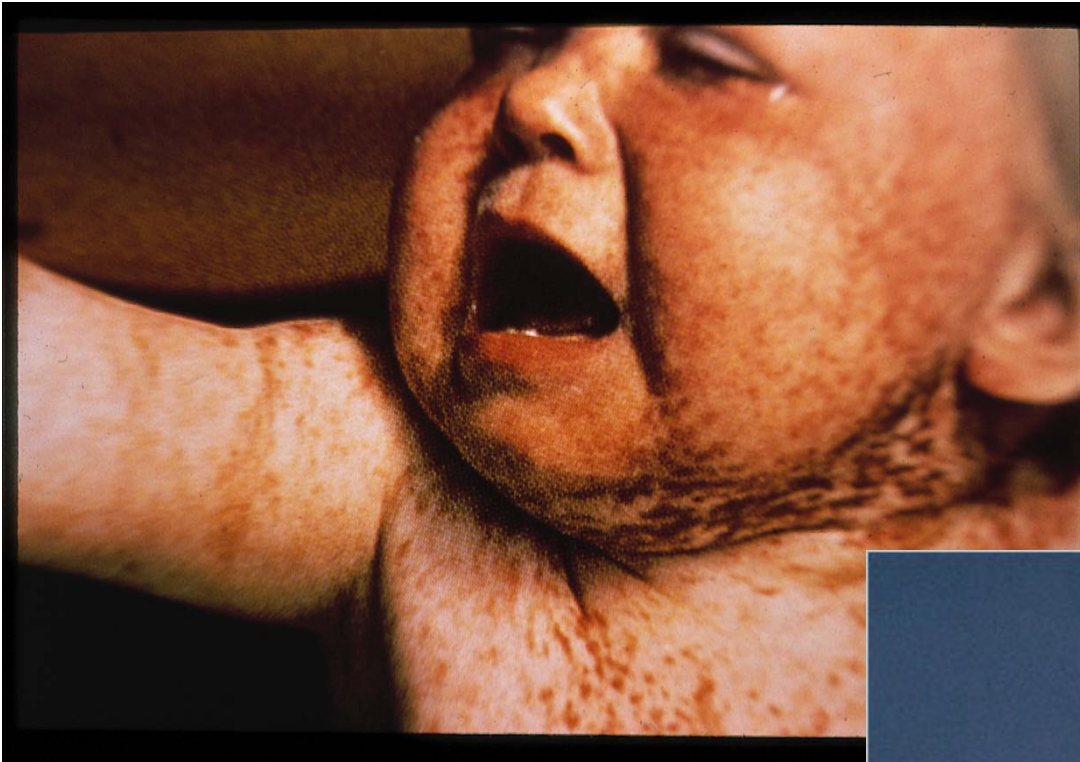
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# Late 20<sup>th</sup> Century: New Variations of Measles

- **Modified measles** – incomplete protection due to blocking maternal antibody, exogenous gamma globulin, inadequate vaccine storage
- **Atypical measles** – usually in those who received killed vaccine in 1960's – immune complex disease, multi-organ effects, a different rash
- Measles in the compromised host
  - Increased measles severity in immunocompromised
  - Do we give MMR to our HIV-infected children?





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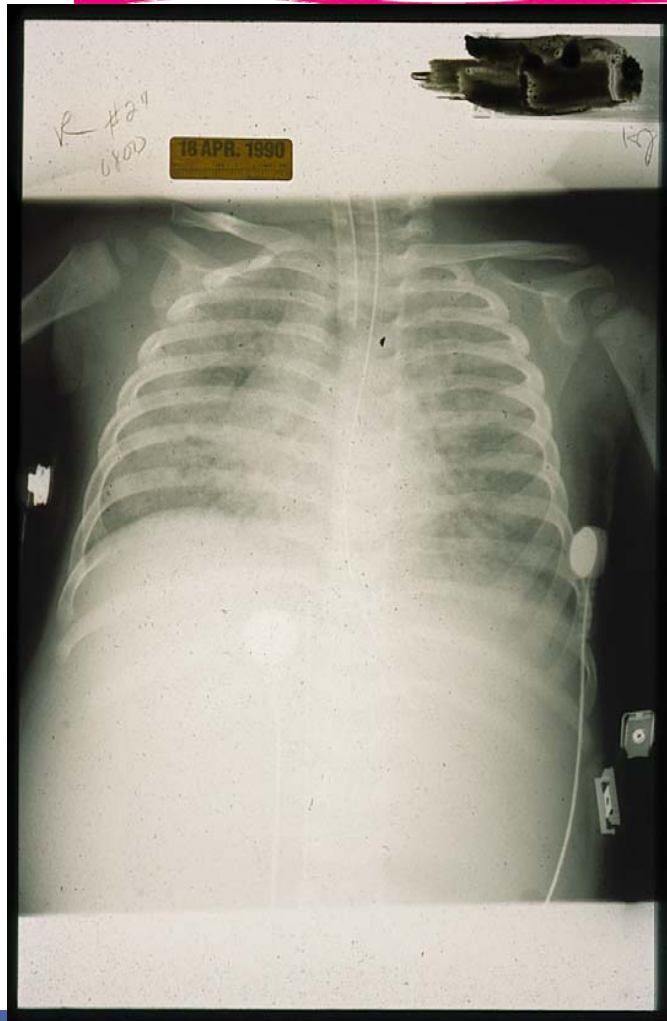
# National Measles Epidemic, 1989-1991

## St. Paul, Minnesota

- **Several early cases of measles in young, unimmunized Hmong children in St. Paul**
- **Early cases had delayed recognition of diagnosis**
- **Rapid proliferation of cases, attempts at passive and active protection w/ IG and vaccine**
- **Ultimately nearly 500 cases with 3 pediatric deaths, all from pulmonary complications**
- **Recognition of very poor immunization rates in St. Paul, especially in the Hmong community**
- **Late phase of epidemic involved other unimmunized and once-immunized children**



# Case Example – April, 1990

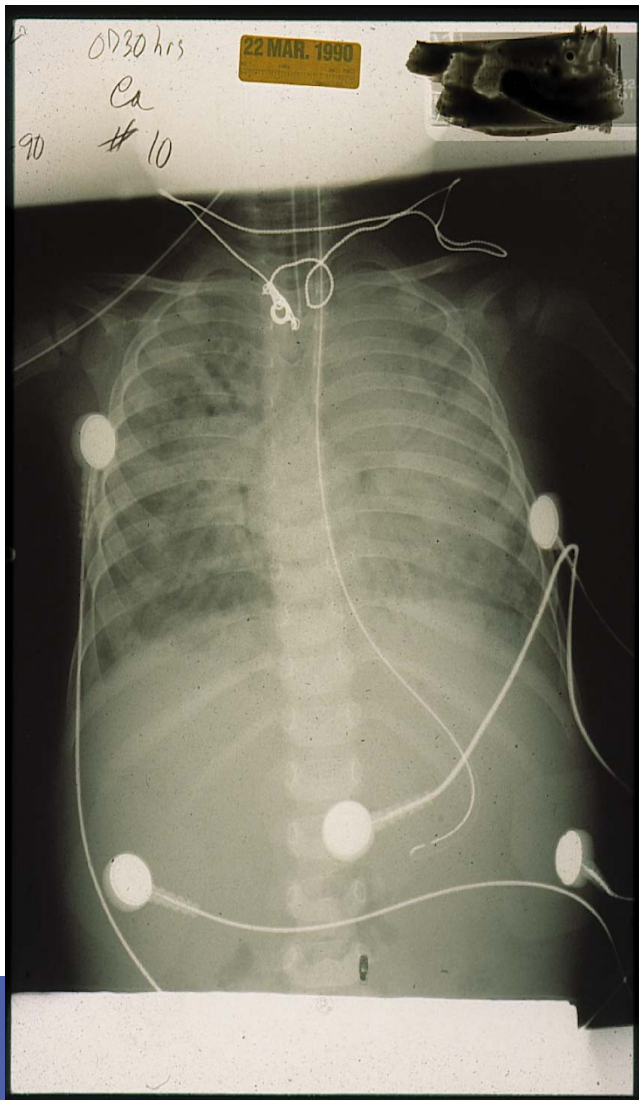


- A 12 month old male was admitted with classic measles symptoms and respiratory distress
- Despite sustained, vigorous ventilatory support, the child died from respiratory failure





# Case Example, Twins – March, 1990



- 18 mo old female, one of identical twins, had usual measles symptoms, then respiratory failure
- After protracted hospitalization, she was discharged on supplemental oxygen
- March, 2009, received lung transplant



# Lessons from 1990 St. Paul Measles Epidemic

- **Recently immigrated populations with low immunization levels are at high risk**
- **Low immunization rate may be a major contributing factor in spread of disease (1989: state MMR 82%, St. Paul pockets 20%; 2011: state 65%, Mpls pockets 30%)**
- **Realized provider missed opportunities, parental confusion, complacency**
- **Epidemic risk is enhanced by living in crowded urban dwellings, exposure to international travelers, diagnostic delay, lack of early aggressive containment measures**
- **WE NEED TWO MMR'S RATHER THAN ONE (initiated late 1989)**



# Measles: Differential Diagnosis

- Kawasaki Disease
- Adenovirus
- Parainfluenza/RSV
- Other resp. viruses
- Scarlet fever (GrA Strep)
- Drug eruptions
- Erythema multiforme
- Rubella
- (Varicella)
- (Rocky Mtn Sp. Fever)
- (Enterovirus – esp w/ aphthous stomatitis)
- (Infectious Mono)
- (Fifth Disease)
- (Roseola)





# Kawasaki Conundrum



- High, prolonged fever
- Bilateral conjunctival injection occurs
- Rash with Kawasaki Disease may be morbilliform
- Mucosal involvement is common



# Kawasaki Disease vs. Measles



**Prominent respiratory features make a strong argument against Kawasaki Disease**

**A normal or near-normal ESR almost excludes consideration of Kawasaki Disease**



# Other Clinical Points



- **Adenoviral infections (“pharyngoconjunctival fever”)** usually have more prominent pharyngitis, less rash, less watery eyes
- **Parainfluenza and RSV** have infrequent rash and mucosal features
- **Scarletiform rash** is usually fine, diffuse, “sandpapery” and associated with strep infection



# Worldwide Eradication Plans 1990-2010

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- Annual deaths worldwide from measles dropped below 1 million in the 1990's, below 800,000 by 2000.
- By 2010, estimated deaths were hoped to be below 100,000 (evidence of plateau in #)
- Continued vigorous immunization efforts should continue steady reduction



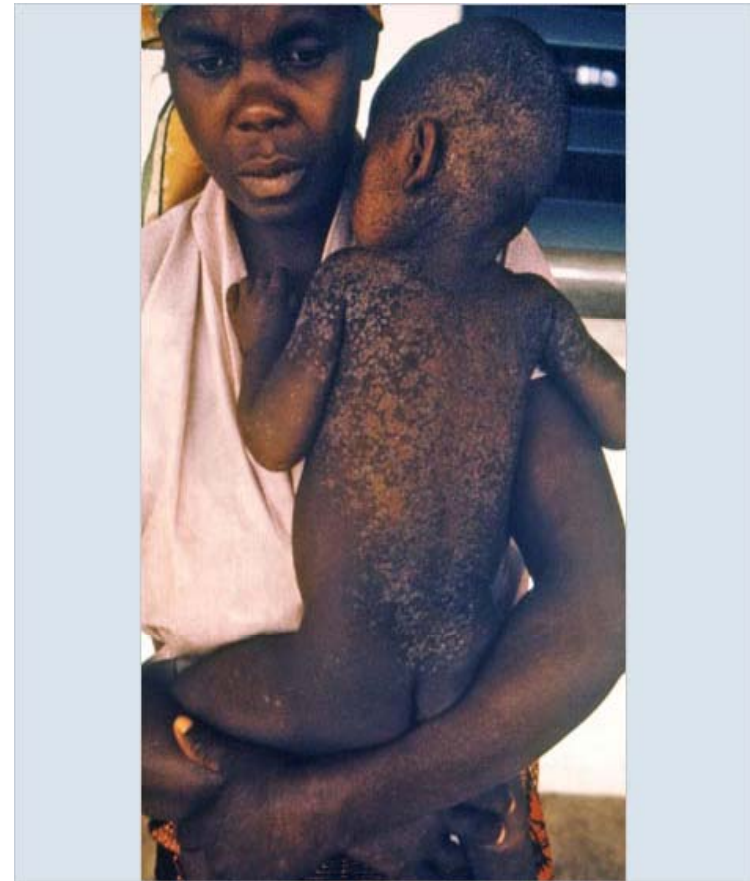
# 2011 Measles in Minneapolis

- **As of March 30, 14 confirmed measles cases, all in Hennepin County. 8 Hospitalized. No deaths**
- **Ages 4 mo – 51 years**
- **Vaccine status:**
  - 4 cases too young to be immunized
  - 6 were of age but not vaccinated by parent refusal
  - 1 unknown
  - 1 vaccinated post-exposure on 1<sup>st</sup> birthday
- **Disproportionate number from Somali community**
  - Somali MMR vaccination rate may be as low as 30%
- **Difficulty in diagnosis in earliest cases**
- **Number of exposed now over 500 children = more cases likely**
- **Exposure identification is rapidly occurring**



# 1998 Twin Story

- Somali mom in Gen Peds clinic with 12 month old for WCC
- Discussing measles disease and need for MMR, provider is stopped by mom
- Interpreter explains this 12 month old was a twin
- They both had measles in Kenya
- This twin survived, his twin died of measles...
- ...She knew the dangers of the disease.



# First 5 Cases at Children's: Preliminary Observations

- High percentage have vomiting
- High percentage have diagnosis of otitis media (→ medication → “drug rash”)
- Diagnoses of atypical Kawasaki Disease, suspected scarlet fever, alternative viral illness with exanthem, aphthous stomatitis
- Rash not always mentioned on the face when present elsewhere
- Peripheral edema possible
- Mucosal lesions often present



# Measles Diagnosis in 2011

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- **THINK OF MEASLES**
- Preferred specimens: throat swab AND urine in sterile cup for PCR, blood for serology IgM
- Nasal washes occasionally used for culture, nasal swab not acceptable.
- DO NOT order measles IgM directly through CPOE. Click order set for Children's "Measles Testing to MDH."





# Treatment of Measles

- **Supportive care is the mainstay**
- **Antiviral therapy not established, occasional use of ribavirin for severe cases (IV)**
- **Vitamin A deficiency is associated with increased mortality**
- **Evidence suggests that vitamin A doses of 200,000 IU/day x 2 days reduce severity, mortality, especially if child is < 2 y.o.**



# Measles: Post-Exposure Prophylaxis

- **Children's protocol for vaccine or passive IMIG is structured according to:**
  - Age (<12 months vs. >12 months)
  - Nature of contact (household vs. other)
    - Time from first exposure -- <72 hours, 72 hours to 6 days, >6 days)

0.25ml/kg for non-immunocompromised

0.5ml/kg in immunocompromised

IMIG (GamaSTAN S/D): Maximum dose 15 ml



# Post-Exposure Prophylaxis

	Time from first exposure		
Age	< 72 hours	72 hours – 6 days	> 6 days
< 12 months	Non-immunocompromised – IG** 0.25 mL/kg IM  Immunocompromised – IG 0.5 mL/kg IM	Non-immunocompromised – IG 0.25 mL/kg IM  Immunocompromised – IG 0.5 mL/kg IM	Monitor for symptoms of measles
> 12 months AND Household contact	Non-immunocompromised - Provide MMR vaccine if no contraindication  Immunocompromised – IG 0.5mL/kg IM	Non-immunocompromised – IG 0.25 mL/kg IM  Immunocompromised – IG 0.5 mL/kg IM	Provide MMR vaccine if no contraindication  Monitor for symptoms of measles
> 12 months AND Non-household contact	Provide MMR vaccine if no contraindication	Non-immunocompromised – Provide MMR vaccine if no contraindication  Immunocompromised – IG 0.5 mL/kg IM	Provide MMR vaccine if no contraindication  Monitor for symptoms of measles



# Measles Outbreak: Containment Strategy

- **Determine if exposed (see list of places, times)**
- **High index of suspicion is crucial; liberal testing**
- **Pre-emptive isolation (child wears mask, placed in negative pressure room) if:**
  - A) **known** exposure and fever OR any of respiratory symptom triad OR rash
  - B) **no** known exposure and fever AND all of respiratory triad (rash may not be present)
- **Mass public immunization in eligible unimmunized**



# Infection Prevention and Control

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- **Extremely challenging due to subtle prodrome that appears similar to other viruses in the office, ED**
- **Most contagious before you really know what you are dealing with**
- **Highly contagious to those sharing “air space”**
- **By the time rash appears, many are likely exposed.**
- **Think of unimmunized siblings, the immunocompromised household member**



# Precautions

- **Routine Airborne**
- **Notify the ER patient coming in with measles, room promptly**
- **Transport patient with surgical mask on or drape blanket**
- **All = Airborne Infectious Isolation is Negative Pressure Room**
- **Keep doors closed**
- **Only immune staff may care for suspect measles cases**



# Health care worker Immunity

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- Immune if born before 1957
- Immune if born after 1957 and have had 2 doses of MMR
- People need to check their own records
- Titers may be drawn if unsure
  
- Disease and vaccine confer lifelong immunity
- If immune, pregnant HCP's may care for children with measles



# MMR Vaccine Guidance

- Give dose one at 12 months of age
- Give dose two 4 weeks later or as soon thereafter
- For example may give 3 year old their second dose
- Adults may need a catch up dose (e.g. born after 1957, exit college before 1989 when dose 2 instituted)
- If dose one is given before 12 months of age (365 days) will not be counted in kindergarten entry and will need to be repeated
- Do not give MMR and Ig together since Ig will block MMR
- No role for Ig or MMR in treatment of acute measles
- Recall children 12 months of age or older who have zero or 1 MMR and bring in for vaccination





# Vaccine Associated “Measles”

- MMR is live vaccine
- Live vaccines can cause “look-alike” rashes
- ~5% of vaccinees will get transient measles rash
- ~7 to 10 days after vaccination rash similar to measles appears
  
- Fever following MMR in 5-15% (to 103 or >)
- Occurs 7-12 days after vaccination
- Lasts 1-2 days
  
- Case: 12 month old in ED 10 days after vaccine with fever, cough runny nose. Mom said hadn't been vaccinated. Work up done, Measles IgM highly positive, urine and throat PCR negative = vaccine associated measles.
- Not contagious. Does not need isolation.



# Ambulatory Care Settings

- **Patients who are being evaluated for measles disease should not be in waiting room areas. If possible, appointments should be scheduled outside regular clinic hours, or at the very end of the day.**
- **Only healthcare workers known to be immune to measles should provide care for patients with known or suspect measles.**
- **Airborne and droplet precautions should be employed.**
- **Examination rooms should not be used for 2 hours after occupied by a patient with known or suspect measles.**
- **Usual procedures for cleaning and disinfecting rooms and patient care equipment are sufficient following measles patients, once 2 hours have passed since the room was occupied.**



# “Limited Social Contact”

- **AKA Quarantine**
- **AKA home bound = no school, no day care, no birthday parties, no Sunday School during incubation period**
- **For those exposed to confirmed case of measles, and no hx of MMR, provide MMR if no contraindication and monitor for symptoms; should “limit social contact” from day 7-21.**
- **Contagion generally begins near beginning of prodrome but most contagious 4 days before and after rash**
- **In vaccinated with 2 doses of MMR, symptom watch and limit social contact at first sign of symptoms.**



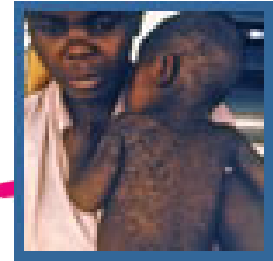
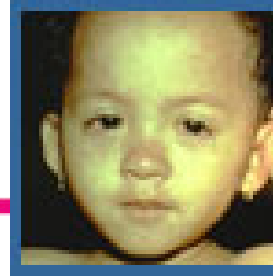
## 2000-2010

# The Beginning of the End of Measles?

- **Smallpox has remained completely eradicated since 1980 – optimism is justified**
- **Polio and measles cases have declined dramatically in this decade, but discouraging setbacks persist**
- **Must dispel myths and misinformation about MMR, promote vaccination as if the child's life depends on it because it does**
- **Every visit is a vaccine visit—don't miss the opportunities to vaccinate**



# Measles Rash

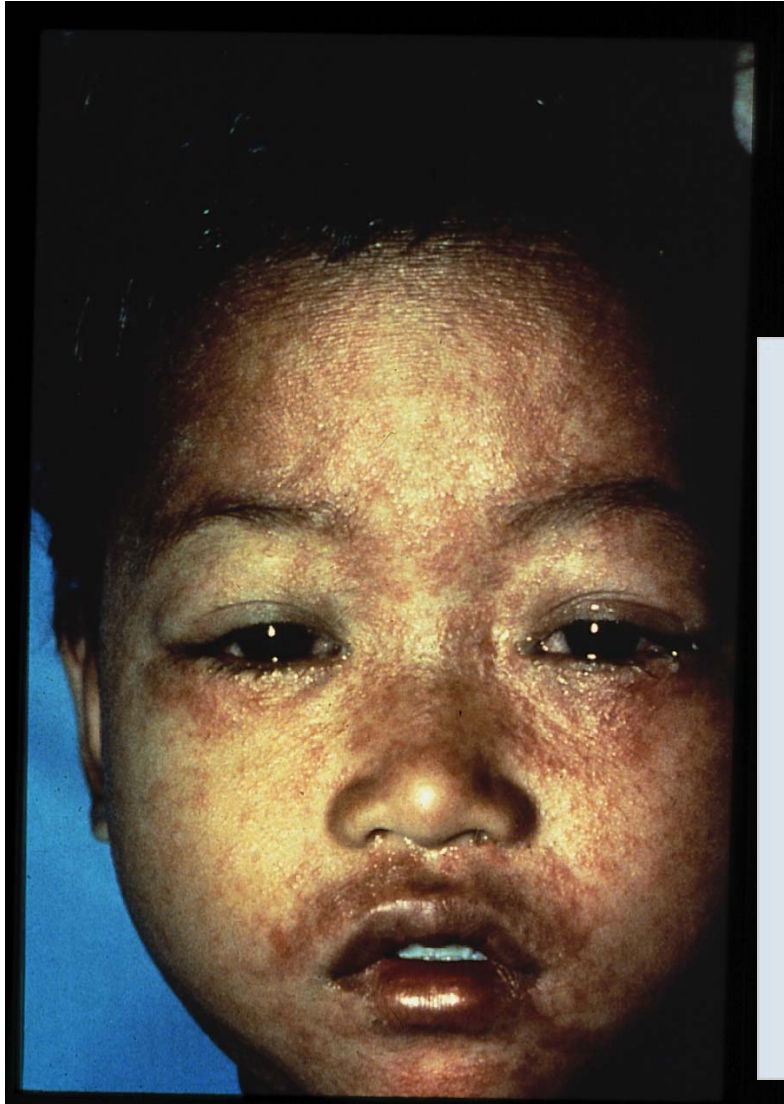


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# Questions?

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# References

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- **Epidemiology and Prevention of Vaccine-Preventable Diseases 11<sup>th</sup> Edition (The Pink Book); p157-176**
- **Minnesota Department of Health Website; Measles update page; last accessed 3/30/11**

<http://www.health.state.mn.us/divs/idepc/diseases/measles/index.html>

