Measles and SSPE

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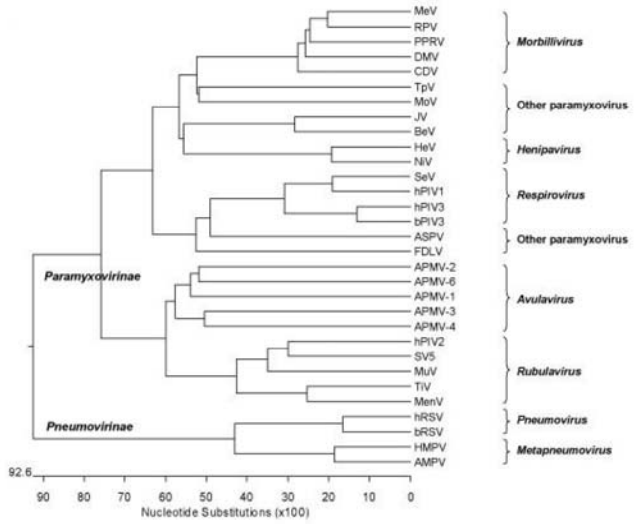
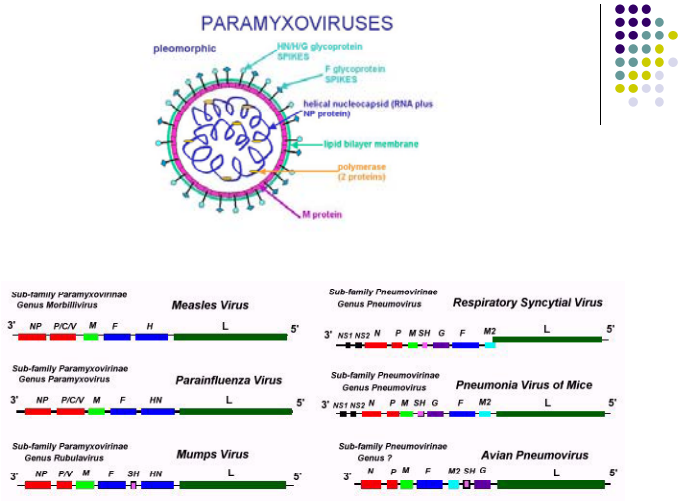




Family

GENUS	MEMBERS	GLYCOPROTEINS
Paramyxovirus	mumps human parainfluenza viruses (HPIV 1-4)	HN, F
Morbillivirus	measles	H, F
Pneumovirus	respiratory syncytial virus	G, F

Measles - Rubeola

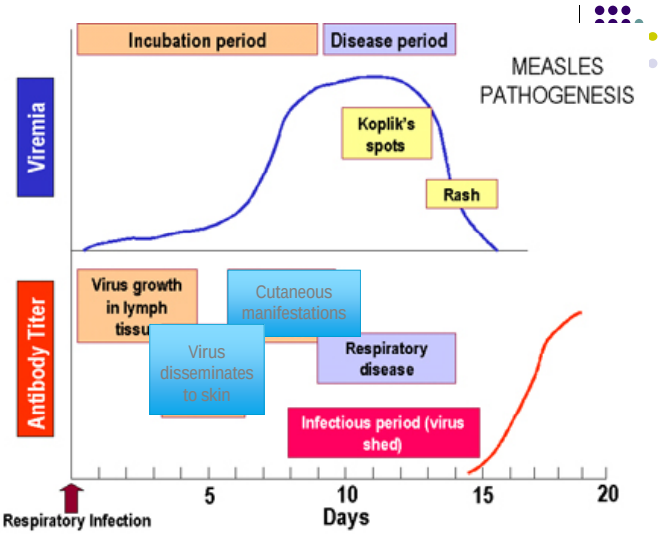
- 1. Organism
  - Measles virus is an enveloped single stranded RNA virus, morphologically indistinguishable from other paramyxoviruses (parainfluenza, mumps, etc.).
  - Member of the morbillivirus genera, the virus has spikes carrying both the hemagglutinin and fusion protein, but no spikes with neuraminidase function.
  - Closely related to canine distemper virus and rinderpest virus of cattle and some partial cross-protection does exist between the viruses.
  - Only one serotype although minor antigenic variants have been identified.

Measles - Pathogenesis

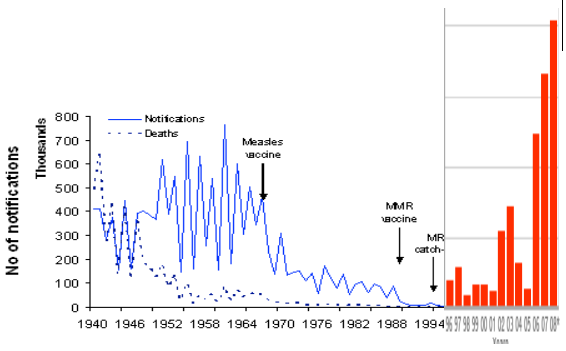
- Usually acquired via the respiratory route and enters the lymphatics through either the upper or lower respiratory tract.
- Infects the lymphoid tissues & and slowly replicates and spreads during the first week post-infection.
- Approximately 7 days post-infection viremia ensues and seeds most tissues throughout the body.
- Clinical manifestations include acute flu-like symptoms including fever, cough, and conjunctivitis. High titers of virus shed via the respiratory tract . Giant-cell pneumonia may be seen (due to cell-cell fusion via the F protein).

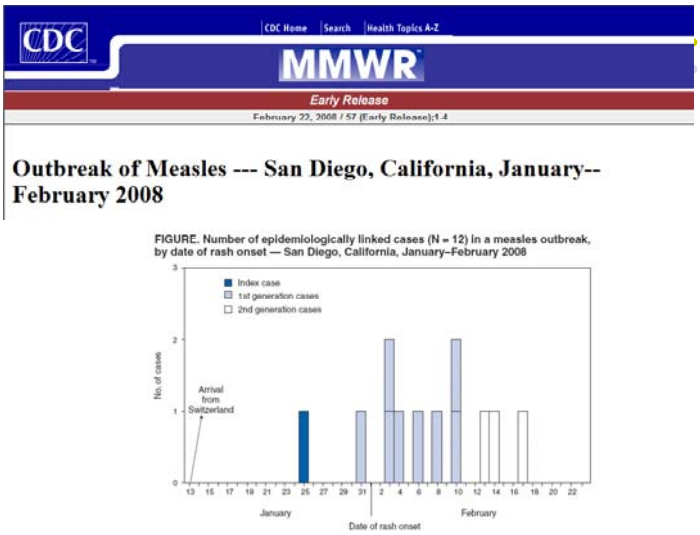
Measles - Pathogenesis

- First clinical manifestation is the formation of Koplik's spots on the buccal mucosa → within a day or two develop maculopapular rash on the face and head → trunk and appendages. Immunocompromised patients do not develop the rash, suggesting a immunopathological mechanism.
- Both circulating antibody and a cell mediated immune response occur. Cell mediated response is primarily responsible for recovery and virus clearing.
- Recovery occurs over the next 10-14 days as the rash fades associated with considerable cell desquamation.



Incidence Measles 1940-2008

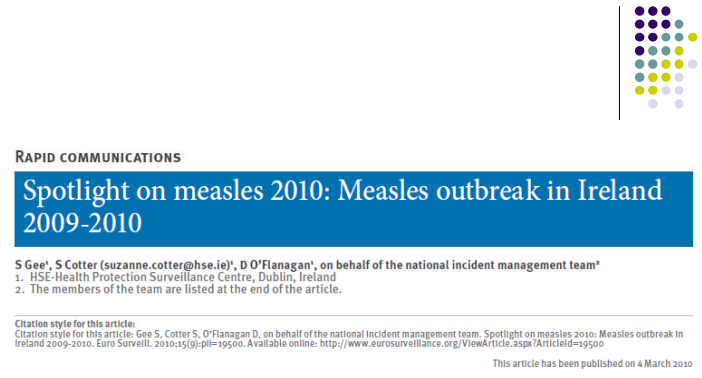


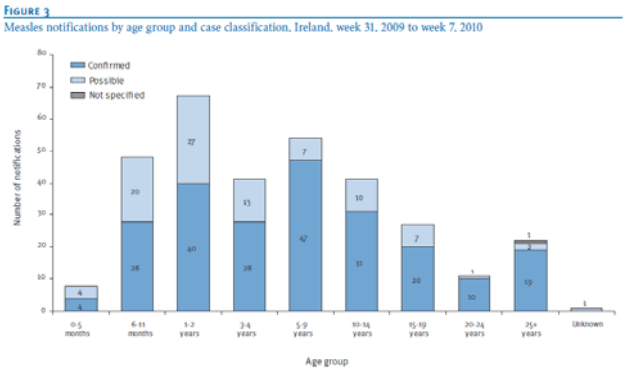


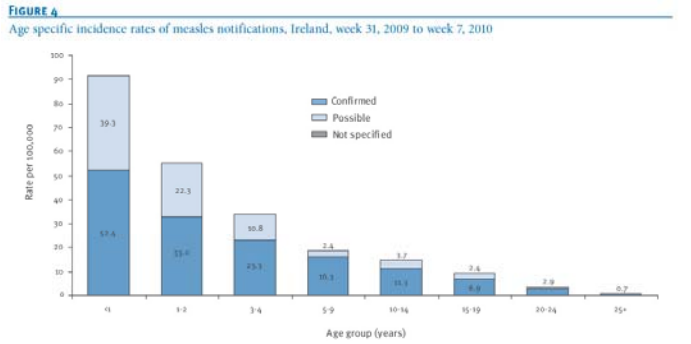
TWO GENERATIONS OF MEASLES CASES WERE IDENTIFIED

- The 1st generation (eight cases) included the index patient's 2 siblings, 2 playmates from his school, and 4children from the pediatrician's office.
- The 2nd generation cases included 3 children from the index patient's school: a sibling of a child from the first generation and 2 friends of one of the index patient's siblings.

- California **allows personal beliefs exemptions (PBEs) to vaccinations required of schoolchildren**.
  - Among the 9 patients aged ≥12 months, including the index patient, 8 were unvaccinated because of PBEs.
  - Approximately 70 children exposed to children with measles in the school, a day care center, the pediatrician's office, and other community settings were placed under voluntary home quarantine because their parents either declined measles vaccination or they were too young to be vaccinated.







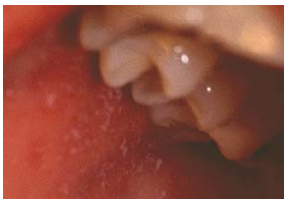
Measles cases are increasing in Ireland, with 320 cases notified since August 2009. Nearly two-thirds of these cases (n=206) were unvaccinated. In the early stages of the outbreak a substantial number of cases were linked to the *Traveller* community with some cases also reported among the Roma community, other citizens from eastern Europe and children whose parents objected to vaccination. By February 2010, there had been considerable spread to the general population.

Measles - Clinical Signs

- a.Early signs are nonspecific and consistent with most respiratory infections (fever, nasal discharge, coughing, sneezing, malaise, etc.)
- b.The first classical sign of measles is the development of Koplik spots on the buccal mucosa followed by the development of the maculopapular rash.
- c.In developed countries measles is generally non-complicated with complete recovery in 10-14 days following development of the rash.

Measles - Clinical Signs (2)

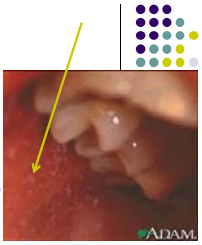
- d.Compromised cell-mediated immune response and malnutrition may lead to more severe disease complications including severe giant-cell pneumonia, secondary bacterial infections (especially pneumonia), and an overwhelming systemic measles infection. Measles is estimated to cause one million deaths annually worldwide.
- e.Vitamin A deficiency appears to decrease local mucosal defenses resulting in many of the complications observed in malnourished patients.



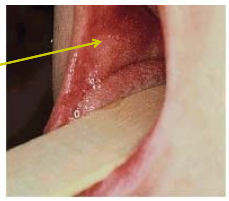
Measles - Complications

- 1.Giant cell pneumonia, a direct result of measles infection of respiratory epithelium, usually most severe in patients with compromised cell-mediated immune responses.
- 2.Measles rarely causes acute encephalitis even though about 50% of uncomplicated measles cases show EEG changes indicative of CNS involvement.
- 3.Post-infection encephalitis occurs in about 0.1 % of the cases, possibly due to the establishment of a low-grade chronic CNS infection.
- 4.Subacute Sclerosing Panencephalitis (SSPE) is a rare (1/1,000,000) complication usually observed in boys with a history of an uneventful measles infection early in life. Following latent period of 1 -10 years a progressive and ultimately fatal neurologic disease develops as a result of a persistent defective viral infection.

Uncomplicated disease



Respiratory tract symptoms: running nose (coryza), cough; conjunctivitis; Koplik's spots on mucosal membranes - small (1-3mm), irregular, bright red spots, with bluish-white speck at center - may get normous number, red areas may become confluent



Uncomplicated disease

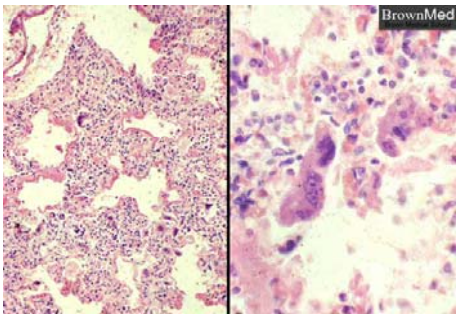
•Maculopapular rash (extends from face to extremities), associated with T-cells targeting infected endothelial cells in small blood vessels).

•Infection is prostrating.

•Recovery usually rapid, cell mediated response important (patients with agamma-globulinemia recover normally).

•Tends to be more severe in adults than children.

Measles Pneumonia



Complications of measles

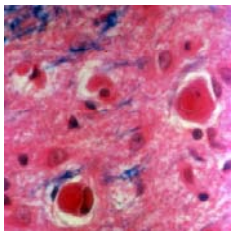
- If patient has an impaired cell-mediated immune response, there is continued growth in lungs leading to giant cell pneumonia (such patients may not have a rash). This is rare, but often fatal.
- Since virus grows in epithelia of the nasopharynx, middle ear, lung, all of these sites may then be susceptible to secondary bacterial infection. Otitis media and bacterial pneumonia are quite common.
- 1 in 1000 cases may get encephalitis a few days after the rash disappears. Most patients (90%) survive encephalitis but there may be complications - deafness, seizures, mental disorders.

Complications of measles

- Outcome is affected by the nourishment of the patient and access to medical care.
- Measles is still a major killer in underdeveloped countries and several studies in areas with severe vitamin A deficiency problems have found that vitamin A treatment of children with measles has resulted in reduction in morbidity and mortality.
- Pneumonia accounts for 60% of deaths from measles.

SSPE

- Very rarely (7 in 1,000,000 cases) the patient may get **s**ubacute **s**clerosing **p**an**e**ncephalitis (SSPE).
- Develops 1-10 years after initial infection. Progressive, fatal disease.
- Risk factors include acquiring primary measles at an early age.
- SSPE associated with defective forms of the virus
- M protein expression frequently absent.



Measles - Diagnosis

- a. Usually made based upon typical clinical signs, especially Koplik spots and maculopapular rash.
- b. Rash is easily identified on Caucasians but may be more difficult to identify on darker-skinned patients.
- c. Classical measles may be misdiagnosed by inexperienced physicians.
- d. Virus isolation is not very sensitive for diagnosis.
- e. Immunofluorescent examination of exfoliated respiratory cells for measles antigen, anti-measles IgM determinations, and hemagglutination inhibition (HI) are the best methods of diagnosis, with immunofluorescence and IgM determinations the best in early cases (prior to well developed antibody response).

Treatment / Prevention

- A live attenuated vaccine is available in combination with mumps and rubella (MMR) and has been effective in producing protective immunity.
- Maternal immunity limits the effectiveness of the vaccine in young children necessitating vaccination at 12 -16 months.
- Even in developed countries, however, the vaccine utilization has been relatively poor at only 55-60% vaccinated.
- The measles virus, as with all paramyxoviruses, is relatively labile and easily inactivated. Spread is by respiratory droplet and the virus is relatively sensitive to dessication. The lipid envelope is easily inactivated by solvents and saponifying agents.

懇請賜教