Childhood illnesses

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Medical Virology,
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Contents of Teaching in Medical Virology Lecture:

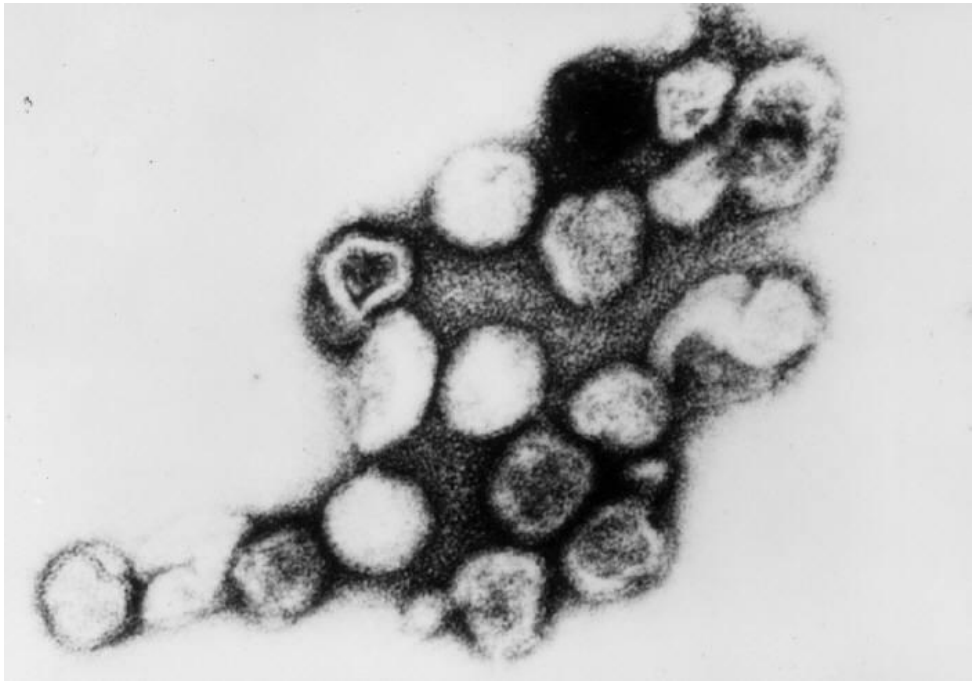
A variety of clinical syndromes in children are caused by viral infections.

- These viruses circulate freely.
- Infections occur predominantly in childhood and are usually followed by life long immunity.

Rubella

Virology:

- *Togaviridae* family, *Rubivirus* genus
  Enveloped, ssRNA, positive sense

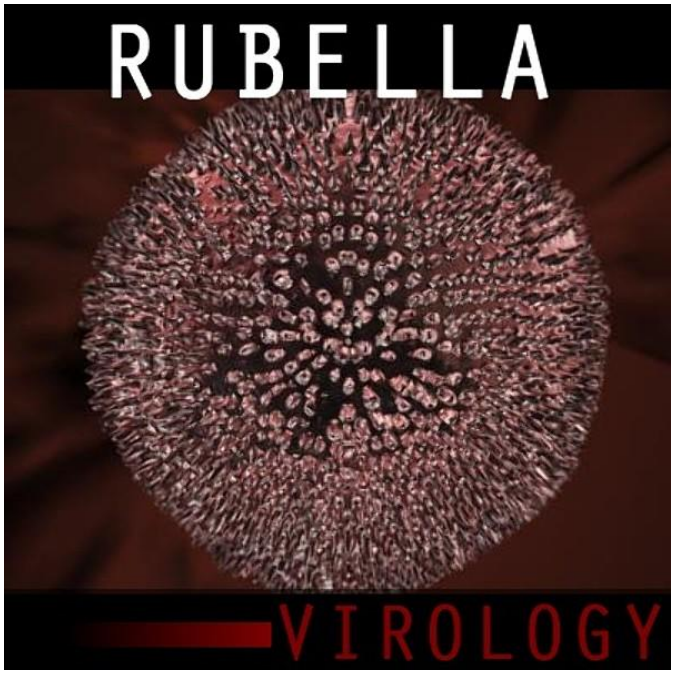


Epidemiology:

- Most people are exposed in childhood.
- Virus is shed in respiratory tract and spread by droplets

Clinical disease:

- Incubation period: 14-18 days
  Rubella causes a mild febrile illness with a blotchy (maculo-papular) rash. Enlarged posterior auricular lymphadenopathy is highly characteristic. This clinical picture is more distinct in adults than in children. Women in particular may develop arthralgia/arthritis during infection. Infection is followed by life long immunity. Women who have rubella in the first trimester of pregnancy are likely to transmit the infection to the foetus. The virus can replicate in foetal cells causing damage to rapidly developing organs. The consequences to the baby depend on the timing of exposure to the virus:
  Before 12 weeks:
  >80% fetuses die (spontaneous abortion) or are born with severe defects to eye (cataracts), heart, brain (micro-cephaly, mental retardation), ear (sensori-neural deafness).
  12-16 weeks:
  Deafness, learning disorders
  >16 weeks:
  No consequence to foetus



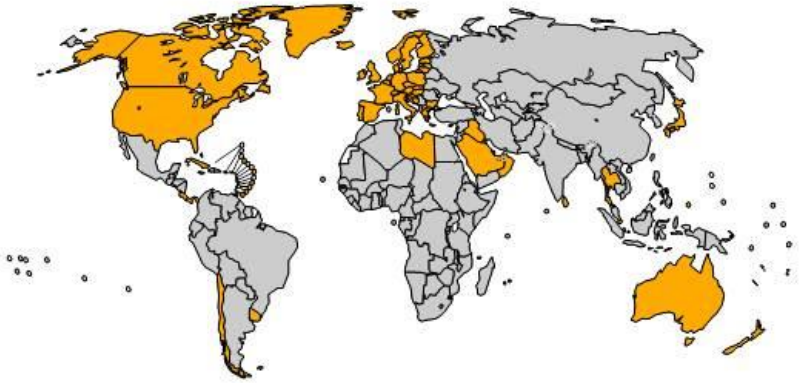
Laboratory diagnosis:

- Acute rubella: rubella IgM
- Congenital rubella: rubella IgM, rubella PCR (urine)
- Immunity: rubella IgG

Rubella

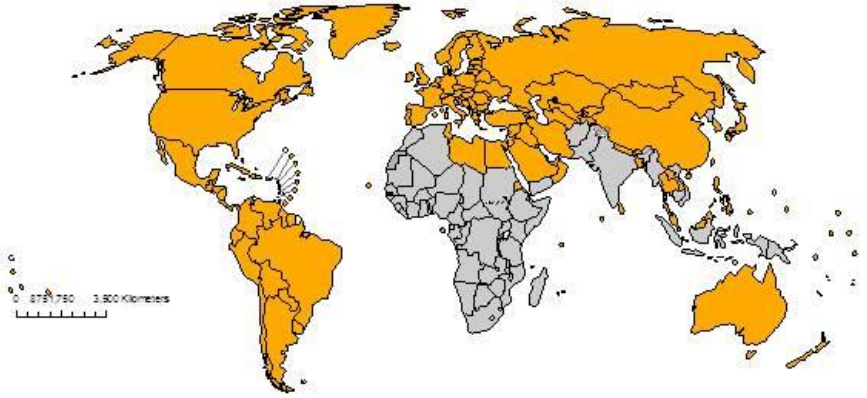
A live attenuated vaccine to rubella was developed in the 1960s.

Countries using rubella vaccine in their national immunization system



1996
65 countries
12% of birth cohort

2012
134 countries
44% of birth cohort



Source: WHO/IVB database and the "World Population Prospects: the 2010 Revision", New York, UN

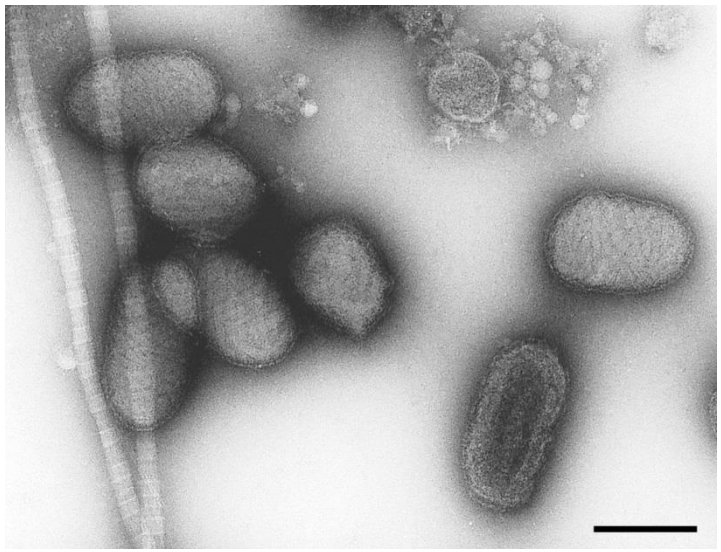
194 WHO Member States. Date of slide: 26 July 2013

WHO

Measles

Virology:

- Morbillivirus (*Paramyxoviridae* family, *Paramyxovirinae* subfamily) Enveloped, ss RNA, negative sense, single serotype



Epidemiology:

- Measles is one of the most infectious diseases known. Infection is spread by respiratory droplets and the airbourne route.
- In the pre-vaccine era, the virus circulated freely in humans. Globally, it was a leading infectious cause of death in children under the age of five years.
- Since the introduction of universal infant immunization, its incidence has reduced dramatically world wide. However, very high vaccine coverage (>90%) is required to stop the circulation of this virus. Ongoing epidemics still occur in under-developed countries.

Measles

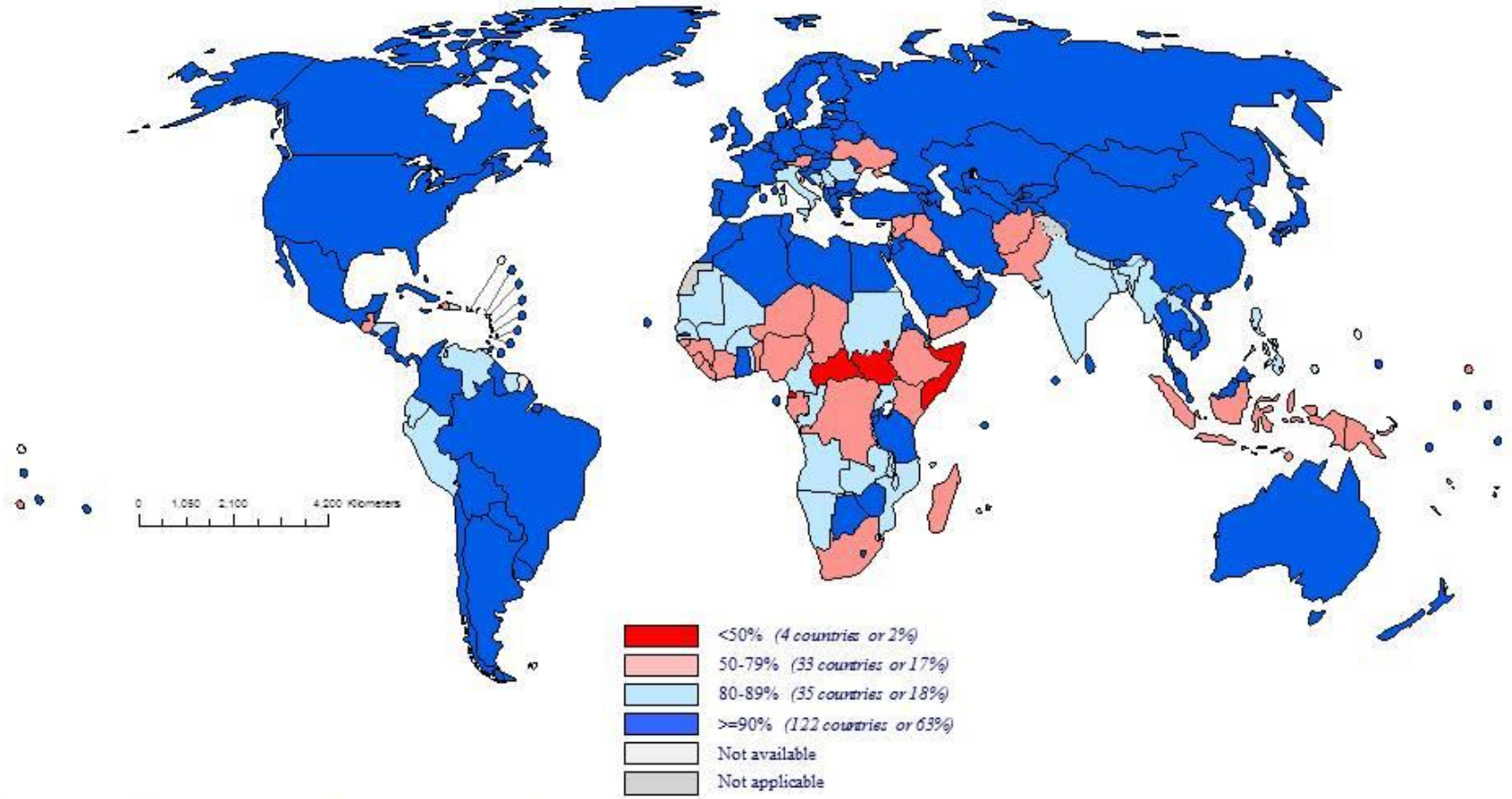
Clinical features:

- Incubation period: 7-14 days
  Illness begins with a prodrome of fever, conjunctivitis, cough, coryza.
- 3-5 days into the illness a macular popular rash erupts on the face and spreads to involve the rest of the body. Patients are most ill during the first 2 days of the rash.
- The virus is highly cytopathic causing widespread damage to respiratory and gut epithelium and transient immunosuppression. These factors put the patient at risk of secondary bacterial and viral complications such as otitis media, pneumonia, diarrhoeal disease. The virus also invades the brain during the acute phase of the illness. Various neurological complications may occur during and after infection (acute measles encephalitis, post-infectious measles encephalitis, sub-acute measles encephalitis and sub-acute sclerosing pan encephalitis).
- This virus is not known to be teratogenic, but intra-uterine deaths can occur in pregnant women with measles.

Vaccine:

- The measles vaccine is a live attenuated virus.
- All infants are required by law to be immunized against measles.
- Two doses of vaccine are given (at 9 and 18 months).
- The vaccine cannot be given earlier because maternal antibody interferes with vaccine replication and no immune response develops.

Immunization coverage with 1st dose of measles containing vaccines in infants, 2014

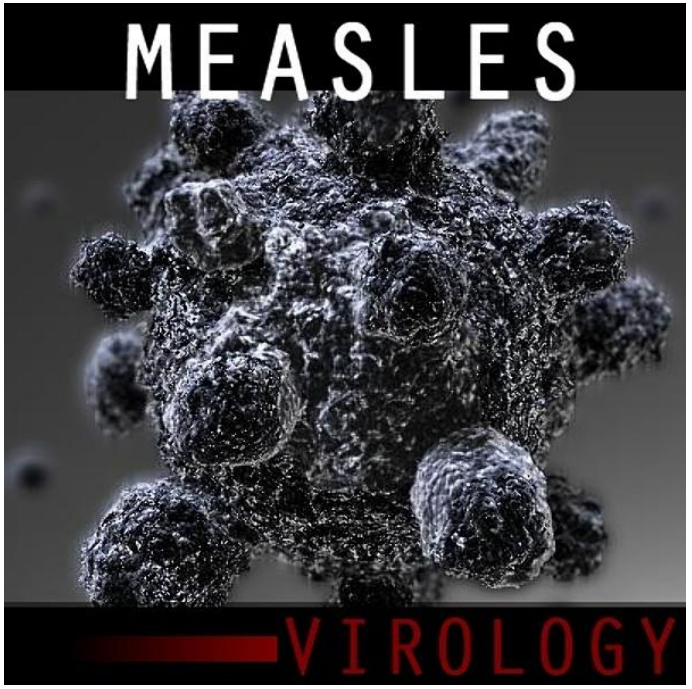


Source: WHO/UNICEF coverage estimates 2014 revision. July 2015. Map production: Immunization Vaccines and Biologicals, (IVB). World Health Organization
Date of slide: 16 July 2015

WHO

Post exposure prophylaxis:

- Non immune individuals who are exposed to a patient with measles have a very high chance of acquiring infection. Measles vaccine should be given to non immune contacts. Individuals in whom vaccine is contra-indicated (infants < 1 year, pregnant women and severely immuno-compromised patients) should be given normal human immunoglobulin.



Laboratory diagnosis:

- Acute infection: Measles IgM, culture or PCR of virus from urine or respiratory secretions.
- Immunity: Measles IgG

Mumps

Virology:

- Rubulavirus (*Paramyxoviridae* family, *Paramyxovirinae* subfamily) Enveloped, ss RNA, negative sense

Epidemiology:

- The highest incidence of mumps is in children between the ages of 5 and 9. However, because the disease is less contagious than other childhood diseases, many people only get it later in life, when they are more likely to be symptomatic - 90% of those between the ages of 10 and 14 are symptomatic, while all those over the age of 60 are.
- Some complications are more common after puberty - notably orchitis, oophoritis, and meningoencephalitis, the latter being 2-3 times more common in males than in females.

Mumps

Clinical features:

- The classic picture is of **parotitis**, which occurs in 95% of symptomatic infections. Subclinical infection is about 30%. The incubation period is 16-18 days.
- Mumps is also a common cause of **aseptic meningitis**. The onset varies from 1 week before the onset of parotitis to 3 weeks afterwards.
- About a quarter of mumps cases in males after puberty are complicated by orchitis, with 20-40% of these being bilateral. There is acute pain and tenderness, with testicular enlargement. Nausea and vomiting may also occur. Late complications include infertility secondary to testicular atrophy (only if orchitis is bilateral). Oophoritis (inflammation of the ovary) is less common in post-pubertal females than orchitis is in males, and it is not associated with female infertility.

Pathogenesis

- Infection is transmitted by respiratory droplets. The primary site for replication is the mucosal epithelium of the upper respiratory tract and the eye. From there the virus spreads to the local lymphoid tissues, and then the primary viraemia occurs, where the virus spreads to other organs - usually the parotid, but also the pancreas, testis, ovary, and central nervous system. A secondary viraemia occurs, with further spread. Virus is excreted in urine and breast milk, but the main source of spread is via droplets from the respiratory system. Interferon appears to play a significant role in the pathogenesis, and stimulates IgG, IgM, and IgA, as well as a cell-mediated response. There doesn't seem to be a higher risk for children with an immune deficiency.

Mumps

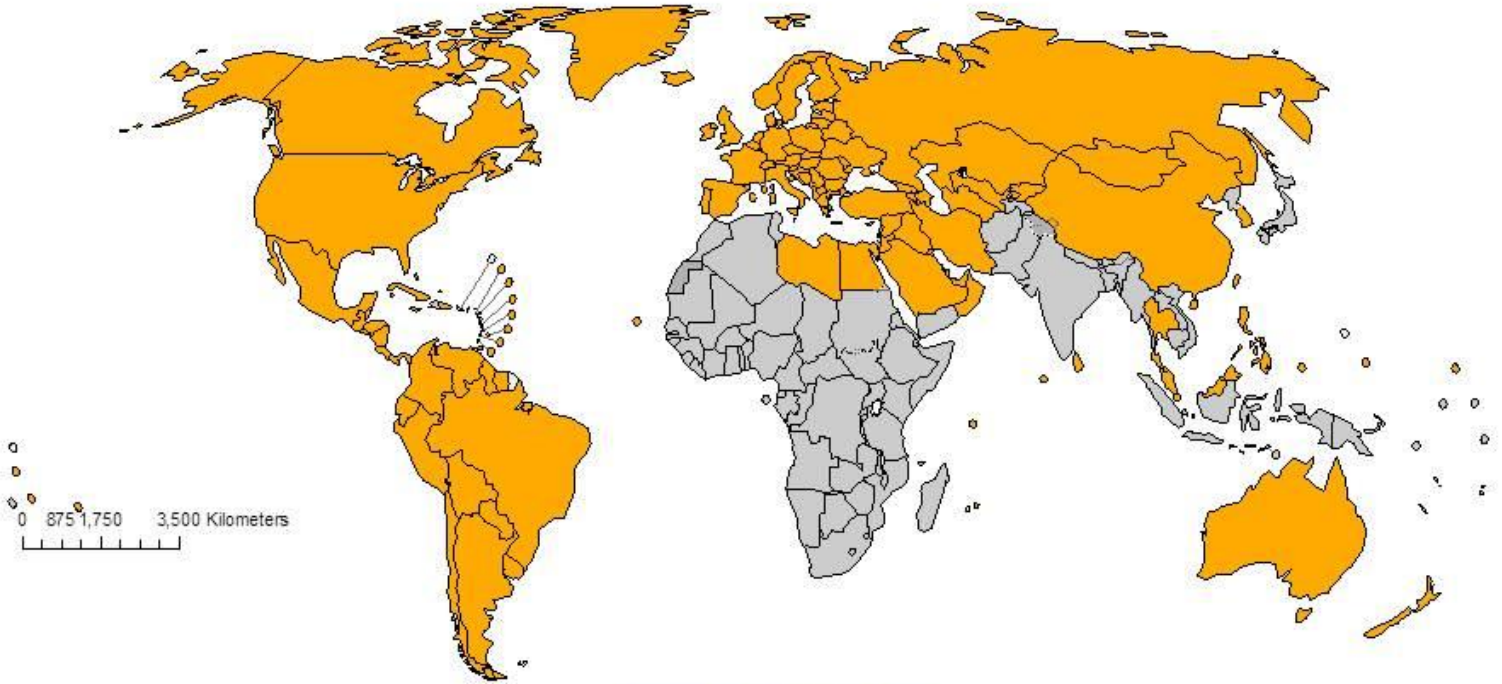
Vaccine:

- The vaccine is a live attenuated virus, and usually forms part of the MMR vaccine (against measles, mumps, and rubella).

Laboratory diagnosis:

- Serology: IgG and IgM; IgG levels correspond to levels of neutralising antibodies.
  Isolation: Mumps can be cultured from saliva and urine.
  Molecular: PCR provides a more rapid diagnosis, and is of use on CSF for a rapid diagnosis of meningitis.

Countries Using Mumps Vaccine in National Immunization Schedule, 2012



No *(74 countries or 38%)*

Yes *(120 countries or 62%)*

Not available

Not applicable

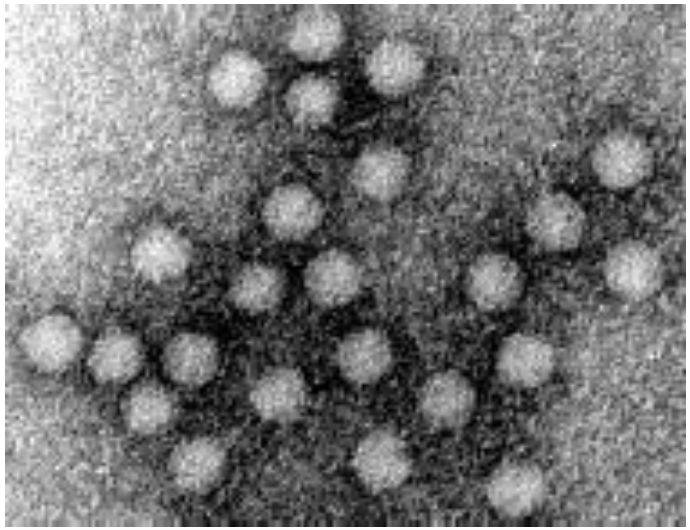
Source: WHO/UNICEF coverage estimates 2012 revision, July 2013. 194 WHO Member States. Map production: Immunization Vaccines and Biologicals, (IVB). World Health Organization
Date of slide: 24 July 2013

World Health Organization

Parvovirus B19

Virology:

- *Parvoviridae* family, *Erythrovirus* genus
  Small, unenveloped, ssDNA virus



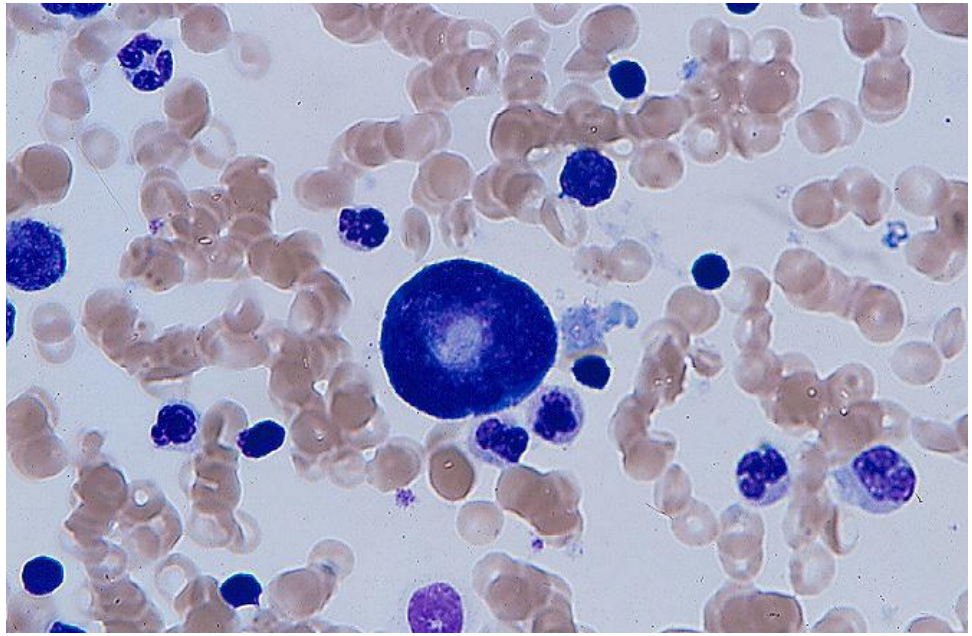
Epidemiology:

- Parvovirus B19 infections occur worldwide.
- Most patients are infected with parvovirus by age 15.
- Infection is more common in the late winter and early spring.
- The virus is transmitted via respiratory droplets and blood products. It can also be transmitted vertically from mother to fetus.
- The incubation period lasts from four to 21 days.
- Patients are no longer contagious once the rash appears.

Complications:

- B19 replicates in red blood cell precursors and transient arrest of red cell syntheses occurs during the acute infection. This is not a problem for healthy people, but can cause an **aplastic crisis** in patients with shortened RBC survival (such as in patients with congenital RBC disorders). In addition, patients with **B cell deficiencies, haematological malignancies** and patients with **AIDS** may fail to clear B19 infection **and infection becomes chronic**. There is ongoing virus replication in RBC precursors causing life threatening anaemia.
- Parvovirus B19 also can cross the placenta leading to **foetal infection**. The foetus is at risk if the mother develops infection during the **2nd or early 3rd trimester** of pregnancy. The virus replicates in the RBC precursors of the developing foetus causing severe anaemia and heart failure (hydrops foetalis). This can result in intra-uterine death. Intra-uterine transfusions can be given to save these babies.

- There is no vaccine.



Aplastic anemia by infecting and destroying early erythroid progenitor cells in human.

Parvirus B19

Laboratory diagnosis

- **B-19 specific antibody testing**: used in immunocompetent patients
  -IgM antibodies will become elevated and remain detectable for 2-3 months after an acute infection
  -Serum IgG indicates the presence of prior infection and immunity

- **Viral DNA testing (via PCR assay):** used for patients who are not immunocompetent and for those in transient aplastic crisis
  -Peripheral blood smear or bone marrow aspirate may show giant pronormoblasts, but this is non-specific

Diagnosis in pregnancy:

- If a pregnant woman is exposed to parvovirus B19, she should be tested for acute infection.
  -IgM levels will be elevated during the acute phase, and IgG will mark seroconversion.

Table 1: Laboratory Diagnosis of Parvovirus Infection

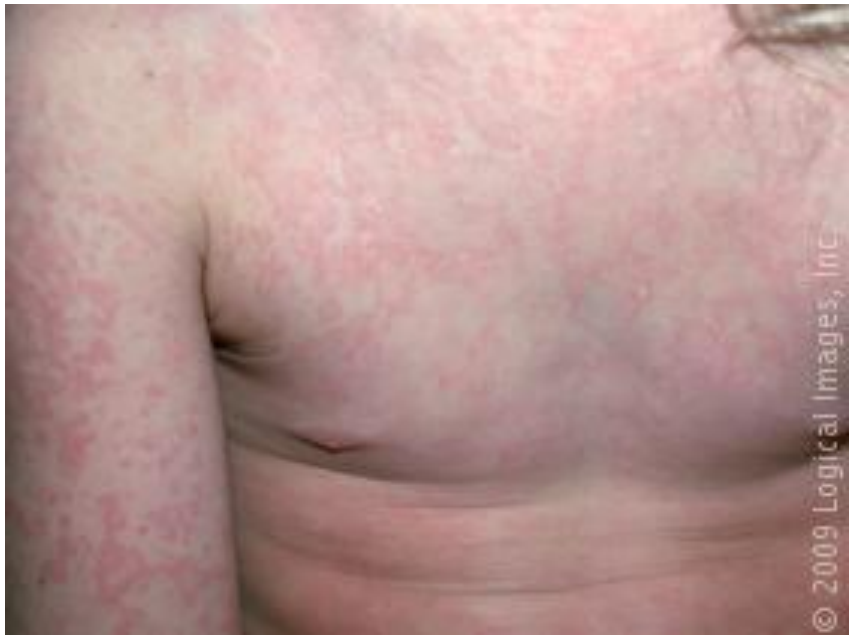
	IgM	IgG	PCR for DNA
Unexposed	--	--	--
Acute Infection (3-7 days)	+++	--	+++
Acute Infection (7-14) days	+	++++	++
Previous Infection	--[1]	+	--[1]
Immunocompromised patient	--	--	++[2]

[1]Increased IgM may be detectable for up to 9 months post-infection; positive PCR results have been observed up to 9 months post-infection as well

[2]Recent versus reactivated versus previous infection with parvovirus in an humorally compromised patient will rely greatly on the clinical history for proper interpretation of nucleic acid testing for parvovirus.

Erythema infantosum, also known as "fifth disease"

- Usually occurs in children ages 4-10.
- Mild prodrome consists of fever, coryza, headache, and nausea.
- Rash

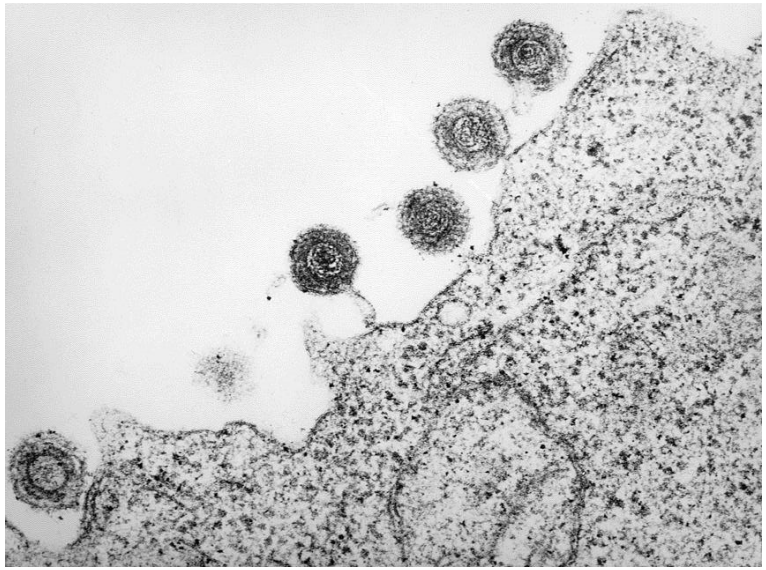


Parvovirus B19 rash in «fifth disease»

Roseola infantum

Virology:

- Human herpesvirus 6
  Herpesvirus family
  Large enveloped dsDNA virus



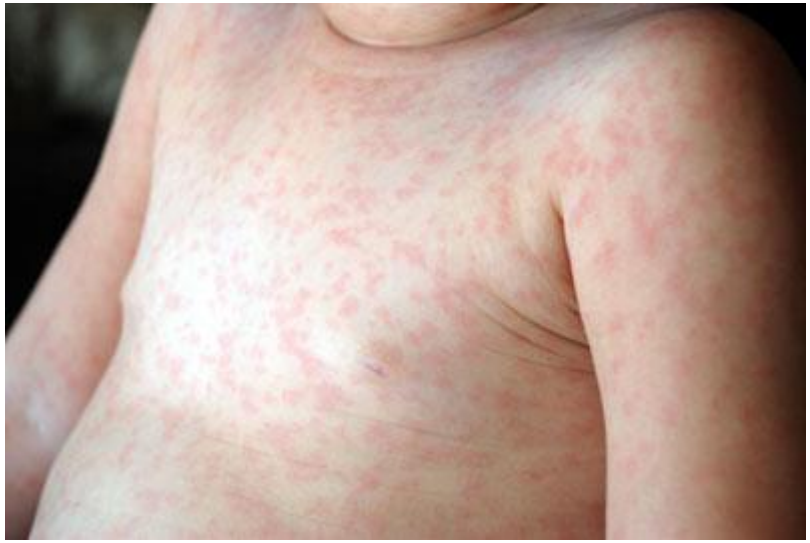
Epidemiology:

- Most people are exposed in the first few years of life.
- Virus is shed intermittently in saliva and body fluids by healthy carriers. It is readily transmitted in families from mother to child or between siblings.
- By adulthood, close to 100% of people have evidence of past exposure (positive anti-HHV6 IgG antibodies).

Roseola infantum

Clinical features:

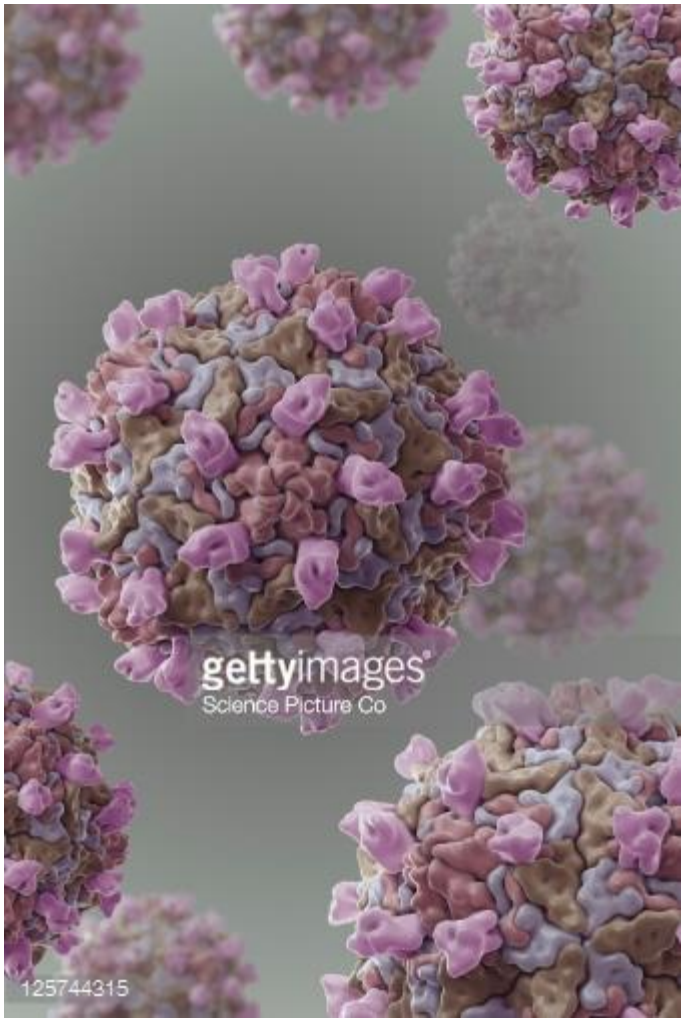
- Primary infection with human herpesvirus 6 in infancy is usually asymptomatic.
- However, in 20% cases infants may develop a high fever, followed by eruption of a generalized macular popular rash as the fever subsides.
- Following the primary infection, the virus persists for life by establishment of latency.



Enteroviruses

Virology:

- *Picornaviridae* family, *Enterovirus* genus
- Small un-enveloped ssRNA (positive sense)
  >100 antigenically distinct viruses (previously classified into 4 groups: polioviruses 1-3, Coxsakie A, Coxsakie B and Echoviruses)



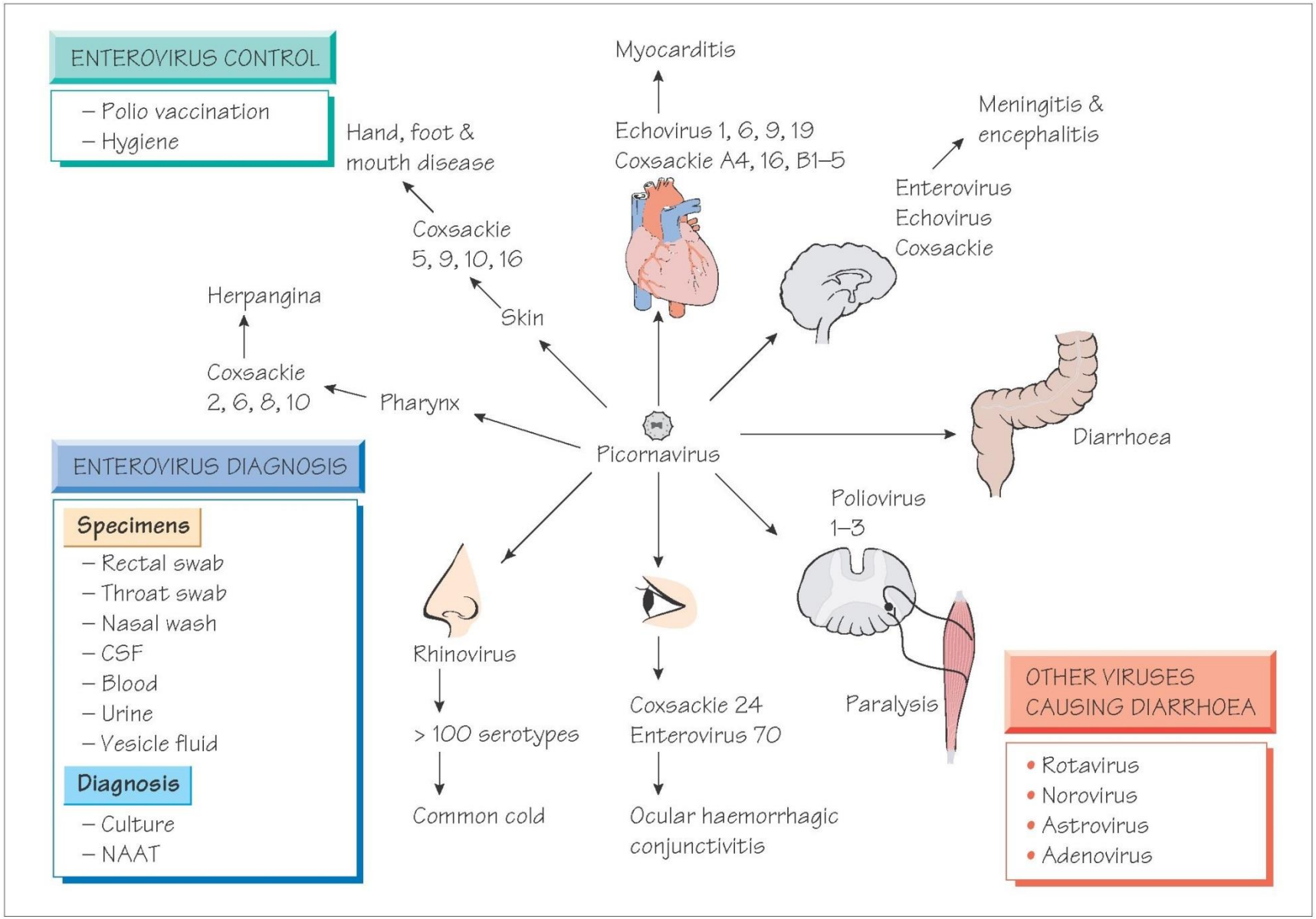
Coxsakie B virus

Enteroviruses

Epidemiology:

- Enteroviruses replicate in the gut and are shed in the stools. Thus transmission is by the faecal oral route.
- Infections have a seasonal prevalence during the summer months.
- Family and community wide outbreaks are common due to the ease of transmission.

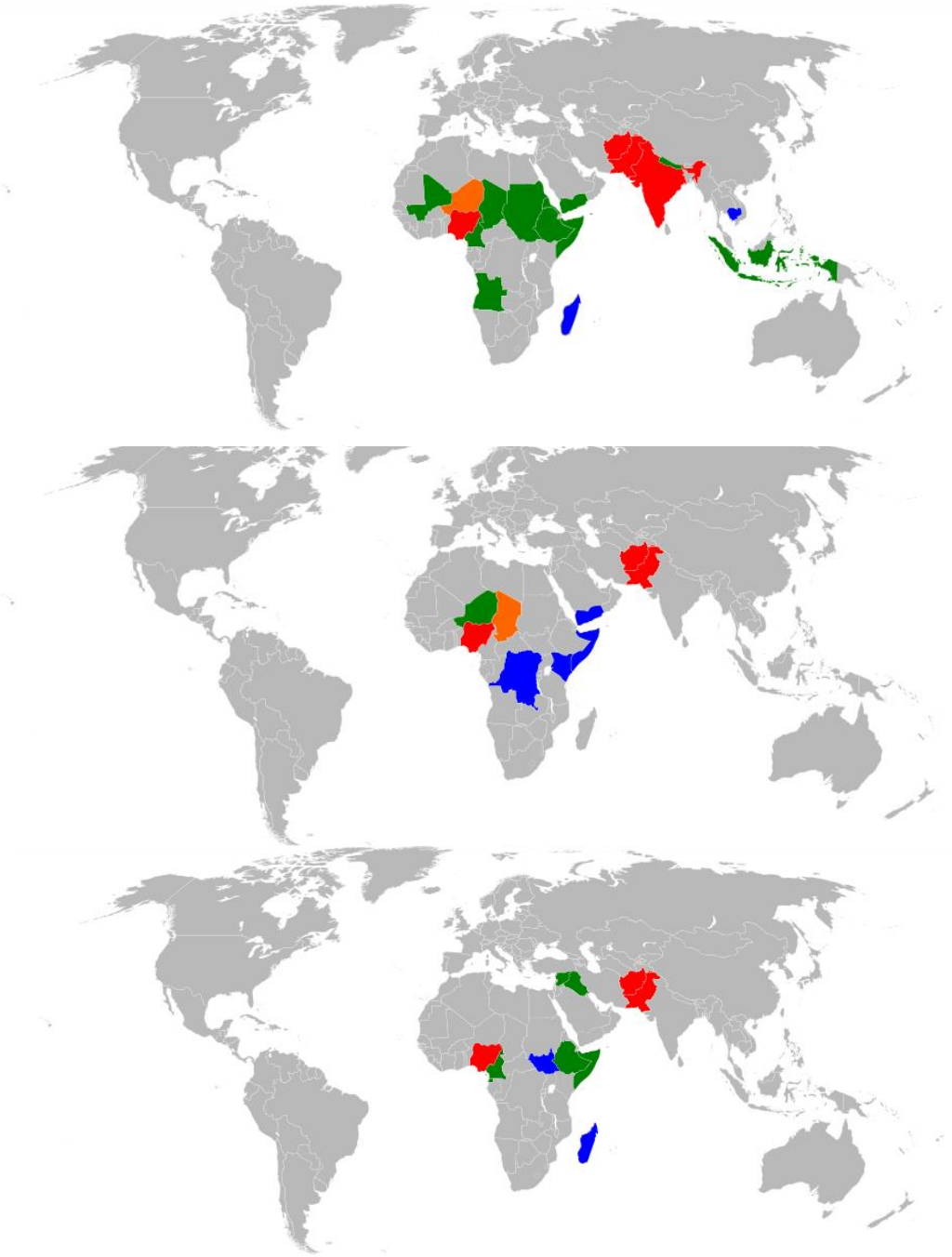
Clinical syndromes of enteroviruses



Enteroviruses

Laboratory diagnosis:

- **Viral Culture:** Virus can be cultured from stool, CSF, throat swabs, blood, and tissue. Highest yields come from stool and throat swabs.
- **PCR:** PCR is commonly used to examine CSF. It is fast and reliable.
- **Serologies:** Serologic tests exist, but due to variations in titers and the large number of enterovirus subtypes, these tests are rarely practical.



Countries with polio cases

in 2005

in 2012

in 2014