the children's hospital at Westmead

Serology: Screening for Vaccine Preventable Diseases

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History of Vaccination

Vaccination

- Immunisation against viral diseases is a triumph of modern science and a triumph of community cooperation and organisation.

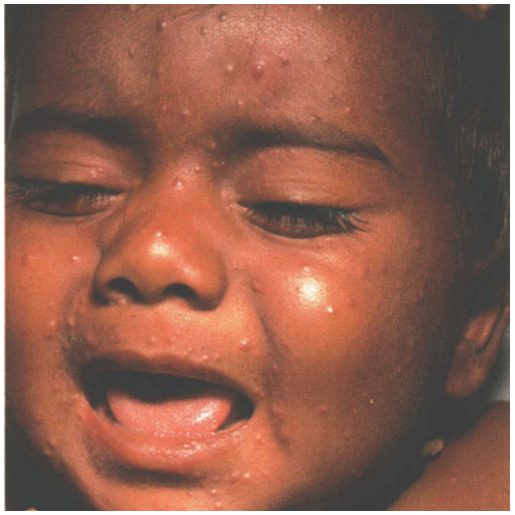
Effect of Vaccination on Populations

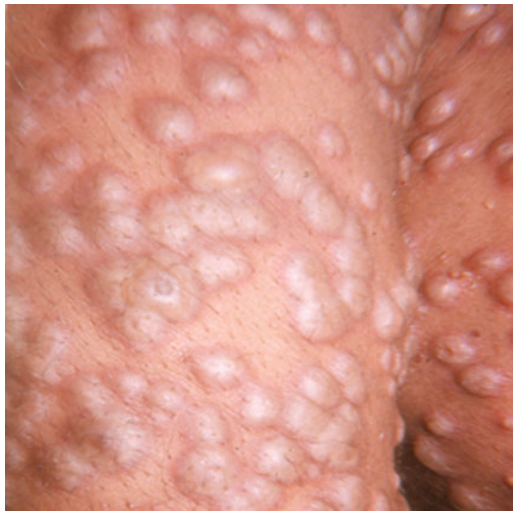
- Smallpox eradicated in 1977
- Poliomyelitis – eradicated from the western hemisphere and many areas
- Measles
- Rubella
- Hepatitis B

Smallpox - Variola

- Eradication of smallpox in 1977
- 180 years after Jenner showed cowpox infection prevented subsequent infection by smallpox

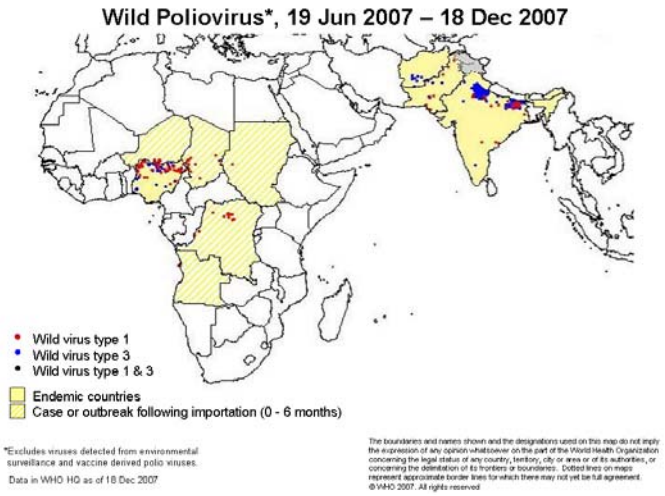
- **Ref: WHO**

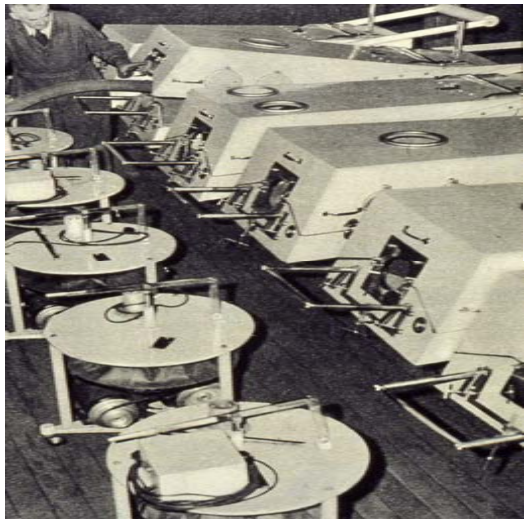




Poliomyelitis

- Estimated that without eradication, more than ten million new cases of polio worldwide would manifest themselves between 2005 and 2040.





What vaccine preventable diseases are there?

Bacterial VPDs

- Tetanus
- Diphtheria
- Pertussis
- Pneumococcus
- Meningococcus
- Haemophilus influenzae B
- Tuberculosis
- Typhoid
- Cholera
- Botulism
- Anthrax
- Plague
- Q fever

Viral VPDs – routine schedule

- Polio 1,2,3
- Hepatitis B virus
- Measles
- Mumps
- Rubella
- Varicella zoster virus
- Rotavirus
- Influenza A and B

VPDs - other

- Hepatitis A virus
- Respiratory syncytial virus
- Rabies
- Smallpox
- Yellow fever
- Japanese encephalitis

What is a vaccine?

Background

- Vaccination or immunisation is the induction or provision of immunity against an infectious disease.
- The immunological basis for vaccination depends upon two central properties of the adaptive immune system; antigen specificity and memory.
- The effectiveness of a vaccine is directly related to its ability to induce immunological memory.

Vaccination

- Active vaccination is induction of host immune response by administration of antigen – long lasting - years.

- Passive vaccination is provision of antibody which provides protective immunity over a relatively short period – weeks to months.

Vaccines

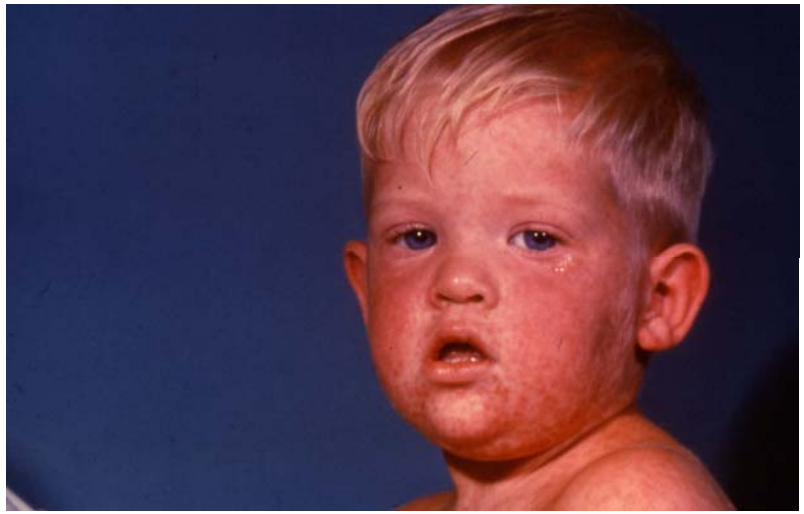
- Vaccines are preparations administered orally or parenterally, which stimulate a specific protective immune response in the recipient without themselves causing diseases.
- Vaccines prevent disease (protective immunity) but do not necessarily prevent infection (sterilising immunity).
- Viral vaccines are either live (attenuated) or killed.
- Attenuated vaccines do not cause disease in immunocompetent individuals.

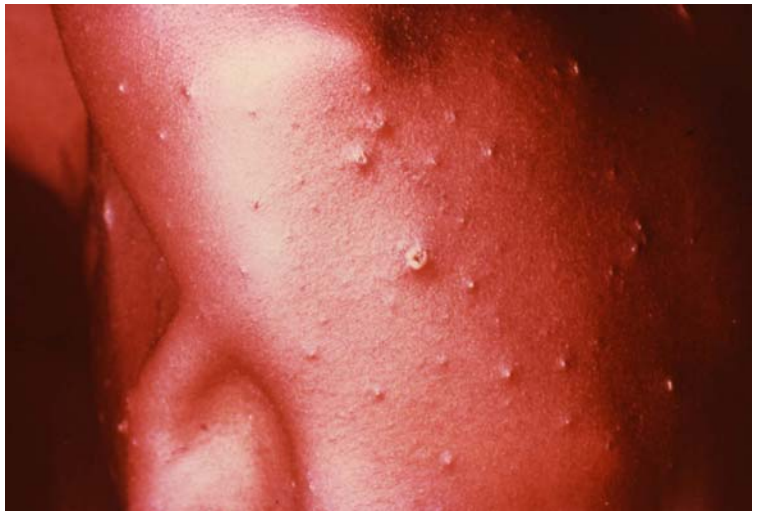
Vaccine protection

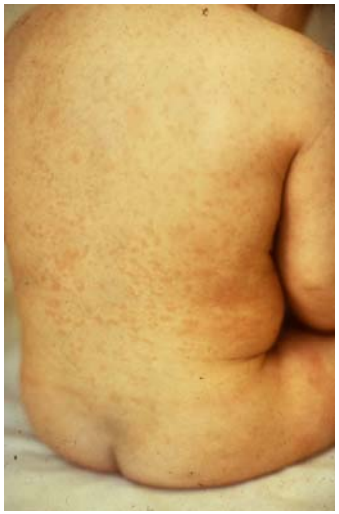
- With protection actual infection may occur and generate a booster response. The infection will be quickly aborted due to immunological memory of vaccine-induced immunity not necessarily located at viral entry e.g. inactivated polio vaccine.

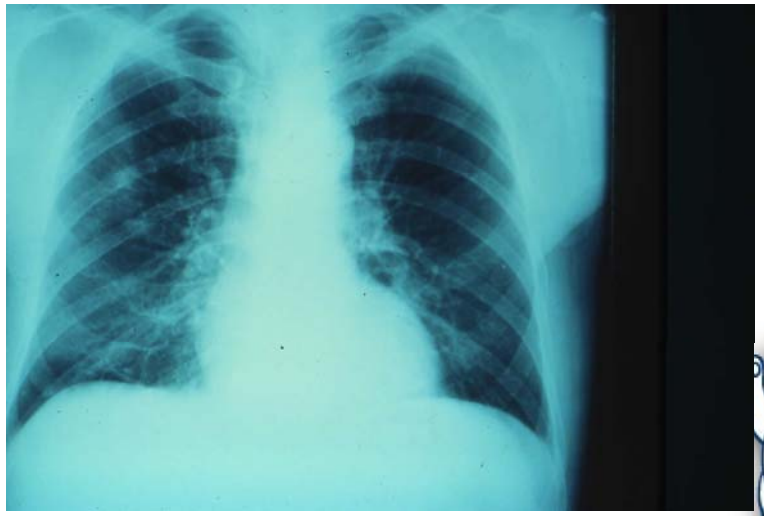
Viral VPDs

Ref:CDC









What is the immunological response?

The "Primary Response"

- The "primary response" occurs after first exposure to an antigen - after a latent period of approx 7 to 10 days circulating antibodies first appear in the blood.
- Ig M antibodies with low affinity appear first and may fix complement, making cell lysis and phagocytosis possible.
- Later antibodies are of IgG with higher affinity.
- The switch for IgM to IgG requires T cell co-operation.

The "Primary Response"

- As the titre of IgG rises (after the second week) the titre of IgM falls.
- IgG antibodies are produced in large amounts and function in neutralisation, antibody-dependent cellular cytotoxicity (ADCC) and fixation of complement.
- The antibody titre usually reaches a peak at about 2 to 6 weeks after infection and then gradually falls.

The "Secondary Response"

- After a second exposure to the same antigen, a heightened memory immune response occurs usually by 4 to 5 days and depends upon proliferation of both B and T cells e.g. measles and varicella.
- This provides immunity and protection against disease.

Mucosal Immunity

- Many pathogens replicate on the mucosal surfaces before host invasion and may induce secretory IgA in the respiratory and GIT mucous membranes (e.g. rubella, polio, influenza).

- IgA is often neutralising, fixes complement (alternative pathway) and lyses some organisms.

Protection

- Some measured immune responses may not themselves confer protective immunity but are correlated with protection and remain as useful markers of protective immunity e.g. IgG to rubella, influenza

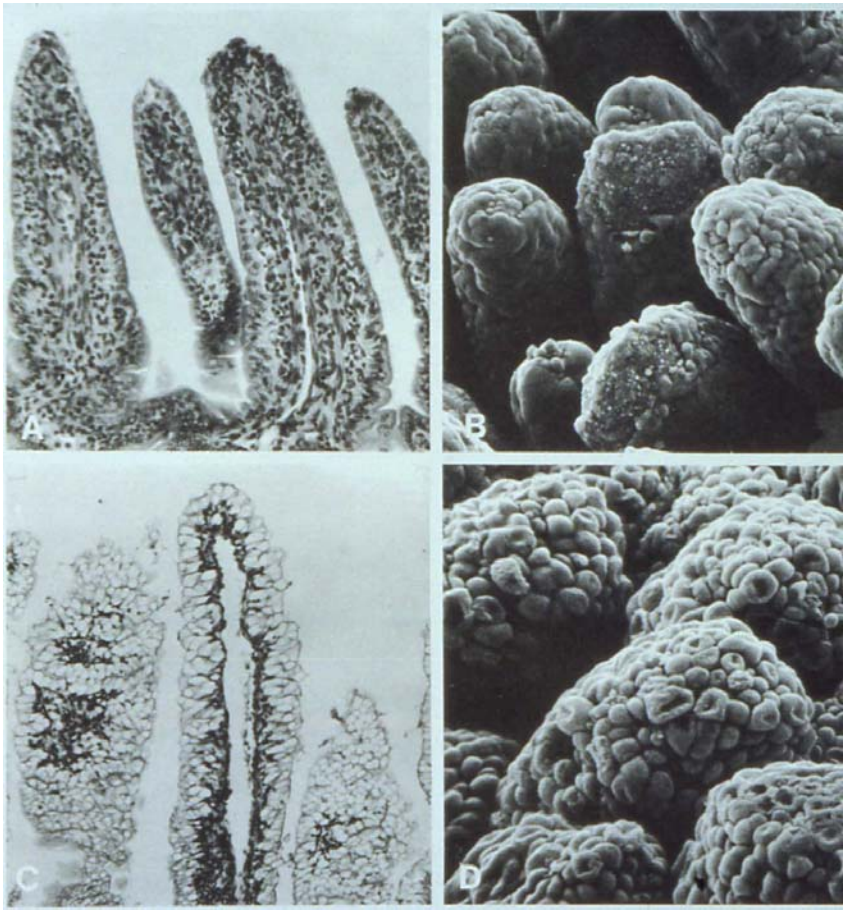
- Parenteral and inactivated vaccines rarely induce mucosal IgA responses.

How do we detect vaccination or infection?

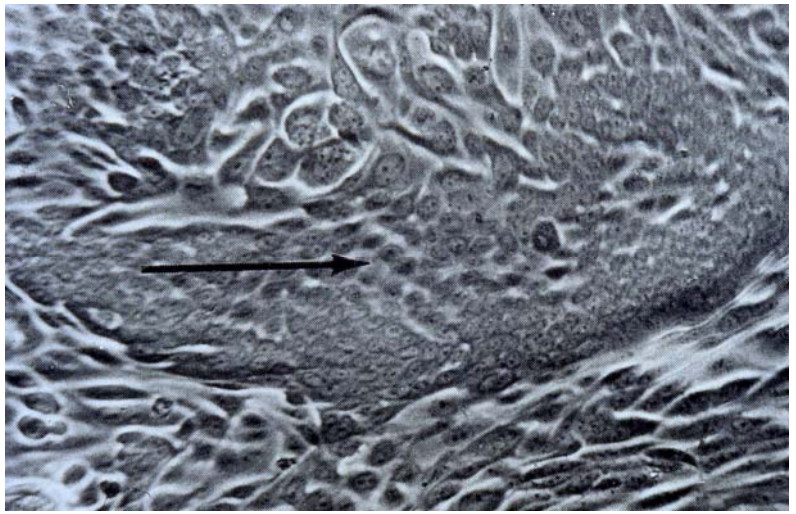
Diagnosis of Infection

- Diagnosis of a viral infection
  - Demonstration of the virus
  - Demonstration of viral antigen or nucleic acid.
- This is in the acute phase of diseases 5-20 days after exposure.
- Demonstration of virus in tissue from affected organs is usually of diagnostic significance
- Exceptions may be adenovirus and enterovirus due to GIT excretion

- Rotavirus



- Respiratory Syncitial Virus



- **Ref: White and Fenner 1994**

Detection of Disease

- Detection of specific antibody has a temporal but not a causal association

- Positive or negative predictive value of result depends on the clinical picture and the prevalence of disease in the population.

Diagnosis of Infection

- Detection of IgM antibodies
- Detection of a rising titre of antibodies in paired specimens
- Detection of a single high titre
- Detection of antigen
- Difficult to distinguish reactivation from primary infection – IgM usually more marked in primary infection.

Diagnosis of Infection

- All laboratory findings have to be interpreted in relation to clinical symptoms and signs.
- The clinician must provide adequate history.
- The laboratory should comment on findings and advise regard further testing.

How do we detect immunity or past infection?

Measurement of Immunity

- Response to a vaccine is usually determined by measuring the appearance and/or concentration of specific antibodies in serum.
- Measles, mumps, rubella hepatitis B, varicella – circulating antibodies correlate with clinical protection, but only measures the humoral arm of immune response.
- Evaluation of persisting antibody has been used to determine duration of vaccine-induced immunity.

Measurement of Immunity

- Absence of detectable antibody is not always correlated with lack of protection e.g. VZV, HBV

- Antibody levels often fall with time (e.g. measles, rubella, HBV) however, revaccination usually leads to a rapid IgG response with little IgM response indicating persisting protective immunity.

Measurement of Immunity

- With some vaccines determining the level of antibody is important to imply protection e.g. rubella.

- Detection of CMI which would be very helpful is a research tool only.

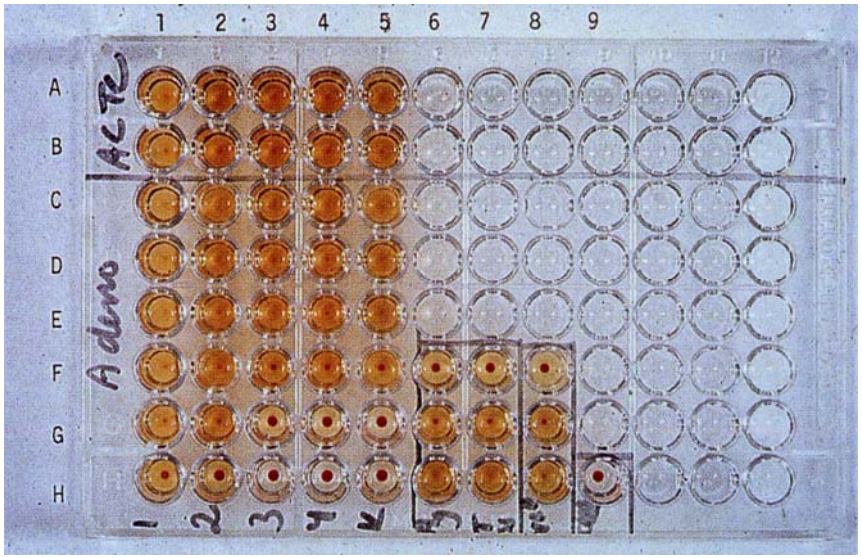
Detection of Vaccine Protection

- Laboratory testing to determine immunity (IgG) is usually different to determining infection (IgM or IgA).
- Most serology performed on serum.
- Anticoagulants added to blood often interfere with assays especially complement fixation.
- A rise in antibody titre may be due to primary infection, reinfection or reactivation.

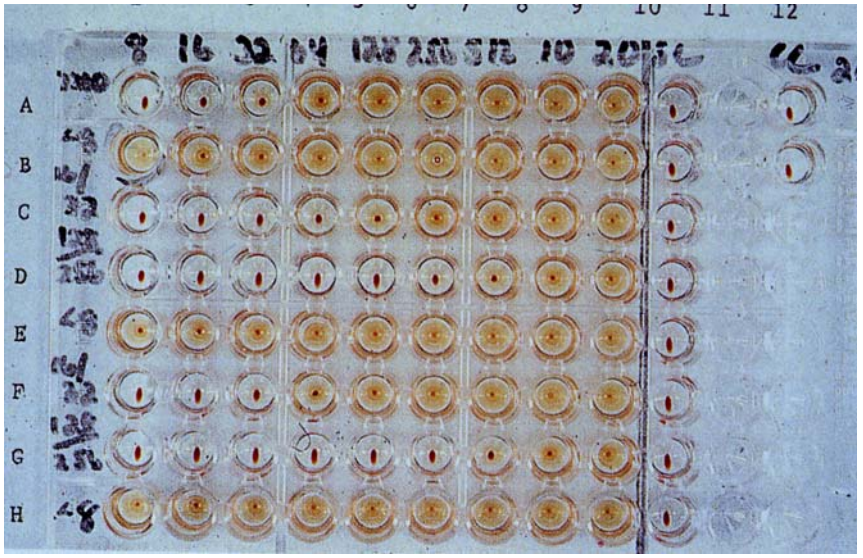
Methods Available

- A variety of methods is available
  - Complement fixation
  - ELISA and relatives
  - Immunofluorescence
  - Haemagglutination inhibition
  - Latex agglutination
  - Neutralisation
- Choice of test depends on the virus, the clinical problem – infection or immunity.
- Demonstration of seroconversion or rising titre requires paired specimens 1-3 weeks apart.

- Complement Fixation Titre (CFT)



- Haemagglutination Inhibition titre (HAI)



What is protection?

- There is some evidence which can be used to determine that an individual will probably have protection from diseases.
- Qualitative detection of IgG e.g. measles, mumps, HAV
  - Detection of antibody correlates with protection
- Quantitative detection of IgG e.g. rubella, HBV

Detection of protection

- Polio 1,2,3 = Neutralising antibody titre
- Hepatitis B virus = HBsAb = >10 IU / mL
- Measles = Measles IgG detected
- Mumps = Mumps IgG detected
- Rubella = Rubella = >10 IU / mL ??
- Varicella zoster = Varicella zoster IgG detected ?
- Rotavirus = Not available
- Influenza A & B = CFT not predictive of protection. Use HAI or Neut.

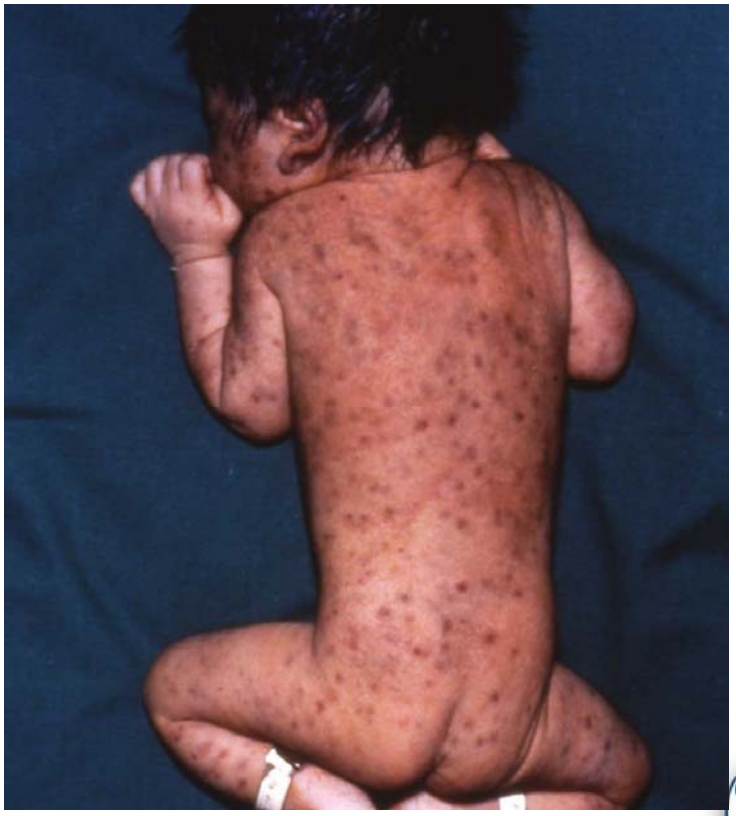
Detection of protection

• Hepatitis A virus	=	Hepatitis A IgG (Total Ab)
• Respiratory syncytial virus	=	CFT not predictive of protection.
• Rabies	=	Rabies antibody – or about to die
• Smallpox	=	Evidence of vaccination within 3 years
• Yellow fever	=	Capture IgM –sensitive (CF, HI) Neutralisation to sort out X-reactions (specific)
• Japanese encephalitis	=	Protection ??

Thank You

Case 1

- Term female infant born to P2G1 mum
- Wt 1.9kg
- Apgars 5^{1}, 7^{5}
- Palpable rash



Case 1

- Mum's serology
  - HBV >100 IU/mL
  - Syphilis screen negative
  - Rubella IgG = 80 IU/mL

Case 1

- Baby's serology
  - HSV IgM – negative
  - CMV IgM – negative
  - Toxoplasmosis IgM negative
  - Rubella IgM – POSITIVE.

Case 1

- How can a baby get congenital rubella if mother has IgG = 80 IU/mL?

Case 2

- Medical staff member of 30 years of age has no history of chickenpox.
- VZV IgG = negative
- Immunised with VZV vaccine, two doses 2 months apart.
- At 3 months VZV IgG = negative.

Case 2

- Is this patient protected against primary varicella zoster virus infection ?