Serology: Screening for Vaccine Preventable Diseases

Alison M Kesson
Infectious Diseases and Microbiology.
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 cooperation.
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 lyases 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

<table>
<thead>
<tr>
<th>Disease</th>
<th>Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis A virus</td>
<td>Hepatitis A IgG (Total Ab)</td>
</tr>
<tr>
<td>Respiratory syncytial virus</td>
<td>CFT not predictive of protection.</td>
</tr>
<tr>
<td>Rabies</td>
<td>Rabies antibody – or about to die</td>
</tr>
<tr>
<td>Smallpox</td>
<td>Evidence of vaccination within 3 years</td>
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<tr>
<td>Yellow fever</td>
<td>Capture IgM –sensitive (CF, HI) Neutralisation to sort out X-reactions (specific)</td>
</tr>
<tr>
<td>Japanese encephalitis</td>
<td>Protection ??</td>
</tr>
</tbody>
</table>
Thank You
Case 1

- Term female infant born to P2G1 mum
- Wt 1.9kg
- Apgars 5¹, 7⁵
- 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?