PRINCIPLES OF VACCINATION

LEARNING OBJECTIVES

At the end of the lecture student should be able to

- Understand how vaccines work
- Understand vaccine classification
- Know about the vaccine types
- Understand commonly used terminology

What is immunization?

Immunization is the process of conferring increased resistance (or decreased susceptibility to infection)

Active Immunity

- Antibodies produced in response to an infection e.g. natural measles virus
- Antibodies produced in response to a vaccine (live, inactivated or toxoid)

Individuals make their own antibodies

Passive Immunity

- Transfer of maternal antibodies through the placenta or in breast milk
  - Passive immunity only lasts for weeks or months. In the case of measles, mumps and rubella it may last up to one year in infants - hence MMR given just after first birthday
- Administration of antibodies (immunoglobulin) collected from actively immune humans or animals e.g. varicella zoster immunoglobulin VZIG
- Individual gains antibodies from another who has produced them

Immunity: Response to antigens
Antigen:
Any molecule, which can be recognized by the immune system as being foreign.

- Micro-organism: bacteria, viruses, parasites, fungi
- Foreign cell: grafted organs, blood transfusion
- A foreign substance: venom

The body will respond through innate and adaptive immunity mechanisms to antigens.

**Innate immunity: main characteristics**
- Rapid – from 0 to 4 hours
- Non-specific – same response to all antigens
- No memory – same response to each encounter

**Adaptive immunity**

If the innate response is not sufficient to eliminate the antigen, more specialized cells the LYMPHOCYTES (T-cells and B-cells) are activated.
**Adaptive immunity: main characteristics**

- **Specificity:**
  - One antibody recognizes only one antigen

- **Memory:**
  - The immune system remembers the infectious agent (antigen) and can prevent it from causing disease in the future.

- **Delayed:**
  - Slow at first encounter (>96 hours)

**Principles of vaccination**
The *immunogenicity* of a vaccine is its ability to stimulate the immune system of the body in such a way that it elicits an adaptive immune response which will help to protect against future infection.

**Principles of vaccination**

- Based on 2 key elements of adaptive immunity:
  - Specificity and Memory

- Stimulation of an individual’s own immune system to produce antibodies by administration of a vaccine

**What is a vaccine?**

A preparation of the causative agent of a disease, specially treated for use in vaccination, in order to induce or increase immunity

**Characteristics of different types of vaccines**

**Live (attenuated) vaccines (1)**

- Contain live (weakened) organisms
- Stimulate the immune response by causing a mild infection with a weakened organism
- No or very low pathogenic potential

- Examples
  - Yellow fever vaccine
  - Measles, Mumps and Rubella vaccine (MMR)
  - Varicella vaccine

**Live (attenuated) vaccines (2)**
Advantage:

- Optimal (close to the naturally acquired) immune response
- Generally the injection of a small antigenic load is sufficient to give long-term protection

Drawbacks:

- Can induce a sub-clinical or mild form of the disease
- Should not be given to the immunosuppressed or to pregnant women

**Killed (inactivated) vaccines (1)**

- Inactivated vaccines = “non-live” vaccines
- Antigenic portions of organisms obtained by:
  - Culture extraction (e.g. pneumococcal polysaccharide vaccine)
  - Genetic recombination (e.g. hepatitis B vaccine)
- Antigenic properties maintained, but unable to multiply in the body (e.g. influenza vaccine)

**Killed (inactivated) vaccines (2)**

- Advantage:
  - Unable to cause disease

- Drawbacks:
  - Less immunogenic
  - Need to couple them with adjuvants or carrier proteins
  - Need for more than one injection or booster

**Toxoid**

- Toxoid = antigen
Toxin (poison) has been modified to be harmless

Examples of toxoid vaccines are diphtheria and tealanus

**Vaccine differentiation**

**Vaccine types**

**Polysaccharide**

- Vaccine contains parts of the complex carbohydrate (polysaccharide) coat of the bacteria which is being targeted

- e.g. 23-valent pneumococcal polysaccharide vaccine – contains polysaccharides (sugar) from 23 different types of pneumococcal bacteria

**Conjugated**

Polysaccharide antigen linked to a protein antigen e.g. Hib, Pneumococcal and Meningococcal conjugated Vaccines

Vaccine modifications

- Adjuvant
  - To enhance the immune response to the vaccine’s antigen
- To carry the vaccine antigen and to slow its release
- To provoke a local inflammatory response

**Measuring response to vaccines**

For many vaccines:

- Vaccination initiates an immune response (immunogenicity)
- The level of the immune response (seroprotective threshold) is well established for some vaccines (e.g., hepatitis B vaccine)
- The generation of an immune response at or above this threshold means that the vaccine will confer protection
- For these vaccines, the immunogenicity also determines vaccine efficacy (as shown in the trials) and clinical effectiveness (as shown by the reduction of disease reported in the population)
• For some vaccines e.g. HPV:
  — Vaccination initiates an immune response (immunogenicity)
  — Identification of the seroprotective threshold requires measurement of antibody levels in vaccinees who develop the disease (vaccine failures)
  — 5-year data shows that HPV vaccine efficacy is almost 100%, as measured by reduction in disease in clinical trials
  — As a result, it is not possible to determine the seroprotective threshold (level below which protection is not conferred)
  — For HPV vaccines, therefore, it is essential to look at vaccine efficacy (reduction of disease in the trials)
  — As cervical cancer can take several years to develop, the clinical effectiveness (reduction of disease in practice) of HPV vaccination for the prevention of cervical cancer will become apparent after implementation of vaccination programmes

How do we measure the immunogenicity of a vaccine? (1)

• Immunogenicity:
  — The capacity of an antigen to elicit an immune response

• Seropositivity:
  — The presence of detectable specific antibodies in the serum as a result of infection or immunisation

How do we measure the immunogenicity of a vaccine? (2)

Seroconversion:
The development of detectable specific antibodies in the serum as a result of infection or immunisation – i.e. a subject moves from a situation in which no antibodies are detectable into one in which antibodies are detectable

Seroconversion comparisons
How do we measure the immunogenicity of a vaccine? (3)

Seroprotection:
The presence of specific antibodies in the serum at least at a level that is known to protect against the disease in question e.g.

- Hepatitis A  ≥ 20mIU/mL (anti-HAV)
- Hepatitis B  ≥ 10mIU/mL (anti-HBV)

Seroprotection comparisons

In this example vaccine B shows superiority in terms of seroprotection for both disease X and disease Y.

Comparisons may be made when two or more vaccines are investigated in the same study (under the same conditions, using the same study design and methods of assessment).

Factors that can influence the immune response to vaccination

Vaccine
Age: *Newborns*:
- Presence of maternal antibodies can inhibit the immune process of vaccination
- Non-response to T-independent antigens

Elderly:
- Weakened immune system

Factors that can influence the immune response to vaccination

- Vaccine
  - Genetic factors
    - According to the individual’s genetic makeup, the immune response to the same antigen can be low or high
  - Nutritional state
    - Malnutrition can be responsible for a relative deficiency of cellular
immunity (T-cell response), (e.g. BCG in some developing countries)

— Underlying Illness
  • Chronic illness may result in different immune Response

**Factors that can influence the immune response to vaccination**

— Vaccine

— Dose and administration route
  • Vaccines should be administered according to the manufacturer’s instructions. Vaccines have been studied by a specific administration route at a specific dose

— Storage conditions (cold chain)
  • Storage must be in line with the licence for the vaccine. For most vaccines this is between +2°C to +8°C because of the risk of loss of potency at higher or lower temperature
  • Expired vaccines: risk of loss of immunogenicity

— Simultaneous administration of immunoglobulins
  • In some cases, the vaccine’s efficacy may be reduced by the injected antibodies

**Importance of good immunization coverage**

**Herd immunity**

— Occurs when the proportion of people immune to an infection is sufficiently high so that transmission of the infection to susceptible individuals is greatly reduced. In that case, outbreaks of the disease do not occur

— Herd immunity helps to protect those who are susceptible and cannot be immunised for whatever reason e.g. immunocompromised, pregnant women (live vaccines) etc.

— Measles:
  • highly infectious disease
over 95% of the population need to be immune in order for that population to have herd immunity

Herd immunity

Animation by courtesy of NHS Immunisation Information, Department of Health
Available online primarily for patients and parents to view at www.immunisation.nhs.uk

Importance of a Successful Immunisation Programme

Conclusion

Importance of vaccination shown by its successes:

- Dramatic reduction in death, deformity and suffering from vaccine preventable diseases
- Dramatic decline in the incidence of diseases (e.g. diphtheria, tetanus, measles, rubella) in countries with high vaccination coverage
- The eradication of smallpox, and poliomyelitis close to eradication
- Continued reduction in healthcare costs due to disease prevention
- Reduction in cost to society e.g. workdays lost

Learning outcomes – summary

Understand how vaccines work
Adaptive immune system
Specificity and memory
Stimulation of immune response

Understand vaccine classification
Live (attenuated) vaccines
Killed (inactivated) vaccines
Toxoid

Know about the vaccine types
Polysaccharide
Conjugate
Adjuvanted

Understand commonly used terminology e.g.
Seropositivity
Seroconversion
Seroprotection
Immunogenicity

<table>
<thead>
<tr>
<th>RECOMMENDED AGE</th>
<th>VACCINE(S)</th>
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<tbody>
<tr>
<td>BIRTH</td>
<td>BCG, Hepatitis B (HBV) OPV</td>
</tr>
<tr>
<td>6 WEEKS</td>
<td>[DTP, HIB, HBV] PENTAVALENT 1 OPV</td>
</tr>
<tr>
<td>10 WEEKS</td>
<td>[DTP, HIB, HBV] PENTAVALENT 2 Oral Polo Vaccine (OPV)</td>
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<tr>
<td>14 WEEKS</td>
<td>[DTP, HIB, HBV] PENTAVALENT 3 Oral Polo Vaccine (OPV)</td>
</tr>
<tr>
<td>9 MONTHS</td>
<td>Measles vaccine (mono)</td>
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<tr>
<td>12 MONTHS</td>
<td>2nd DOSE OF MEASLES</td>
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THANK YOU