Core Topic 4

The different types of vaccines used and their composition

Health Protection Agency

Learning outcome

To have knowledge and understanding of the vaccines used in the national immunisation programme

Learning objectives

- Identify the type (immunoglobulin, live, inactivated, polysaccharide, conjugate) of vaccine used to prevent each disease
- State when immunoglobulin is indicated
- Describe how vaccines trials are carried out before a vaccine is licensed and how safety and efficacy are monitored after they are licensed and in general use
- State the contraindications for each type of vaccine
- Describe the nature and frequency of adverse events and compare these with the complications of the diseases
- Know what intervals need to be observed between doses of different vaccine

Type of vaccines

Passive immunisation

antitoxins and immunoglobulins which provide immediate source of antibody

Active Immunisation

- **Live vaccines**

attenuated (weakened) organism which replicates in the host

- **Killed/inactivated/subunit vaccines**

killed micro-organisms, inactivated toxins or other subunits

Types of vaccine

Vaccine	Examples
Immunoglobulin (IG)	Varicella Zoster IG Human Normal IG Hep B IG, Tetanus IG
Anti-toxins	Diphtheria anti-toxin Botulinum anti-toxin
Inactivated/subunit vaccine	Diphtheria/tetanus/acellular pertussis /inactivated polio/*Haemophilus influenzae* b (DTaP/IPV/Hib) Meningococcal C (MenC), Pneumcoccal (PPV & PCV) Human papillomavirus vaccine (HPV) Hepatitis A vaccine (HAV) Hepatitis B vaccine (HBV),
Live attenuated	Measles, mumps and rubella (MMR), Yellow fever

Passive immunity

Immunoglobulins are concentrated antibody preparations (given IM or IV) which provide immediate short-term protection against disease

Given to individuals who are at high risk of experiencing severe disease or of developing serious complications from the disease

> Most are given to high risk contacts of cases who were exposed during the infectious period and who are still within a window of time during which it can be effective (varies according to infection)
>
> See immunoglobulin guidance in Green Book and HPA Immunoglobulin Handbook for further information

They provide immediate protection but this is short-lasting (only a few weeks or months)

They do not stimulate the immune system to produce any antibodies

Antibody Preparations

Human source – pooled blood preparations from donors

- Human Normal Immunoglobulin (HNIG) (for contacts of Hep A, measles, polio and rubella)
- Varicella Zoster Immunoglobulin (VZIG)
- Hepatitis B Immunoglobulin (HBIG)
- Human Rabies Immunoglobulin (HRIG)
- Tetanus Immunoglobulin (TIG)

Monoclonal

- Palivizumab (to prevent respiratory syncytial virus (RSV) in children at high risk of disease)

Animal source

- Diphtheria anti-toxin (used for treatment of diphtheria - not prevention)

Live vaccines

•attenuated strains which replicate in host

attenuation means the virus or bacterium has been weakened to reduce virulence so it cannot cause disease in healthy people

•act like natural infection

live vaccines are the closest to actual infection and therefore elicit good, strong, long-lasting immune responses

Live vaccines

Advantages

- Single dose often sufficient to induce long-lasting immunity
- Strong immune response evoked
- Local and systemic immunity produced

Disadvantages

- Potential to revert to virulence
- Contraindicated in immunosuppressed patients
- Interference by viruses or vaccines and passive antibody
- Poor stability
- Potential for contamination

Inactivated vaccines

Either:

•suspensions of whole intact killed organisms

e.g. whole cell pertussis, influenza, rabies, HepA

Or:

•acellular and sub-unit vaccines

contain one or a few components of organism important in protection

e.g. acellular pertussis vaccine contains between 2-5 components of the whole cell pertussis bacteria

e.g. diphtheria toxoid

e.g. Hib polysaccharide

Inactivated vaccines

Advantages

- Stable
- Constituents clearly defined
- Unable to cause the infection

Disadvantages

- Need several doses
- Local reactions common
- Adjuvant needed

keeps vaccine at injection site

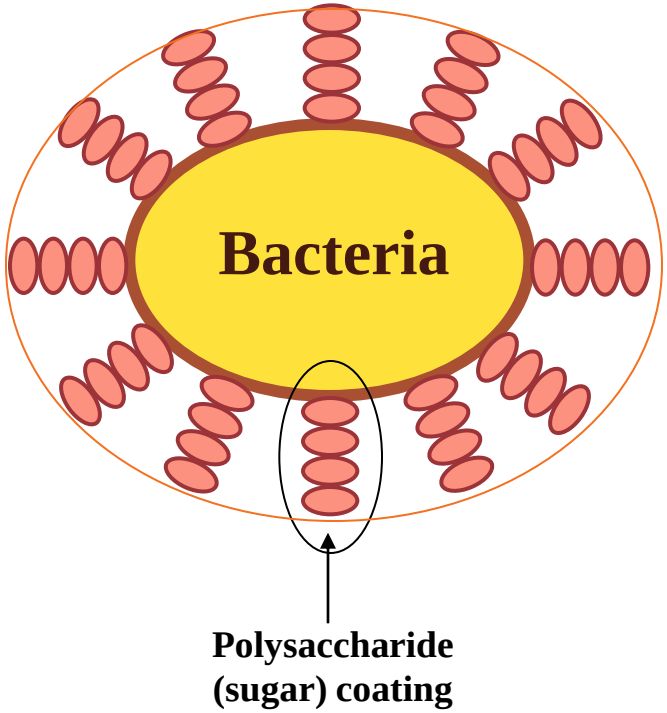
activates antigen presenting cells

- Shorter lasting immunity

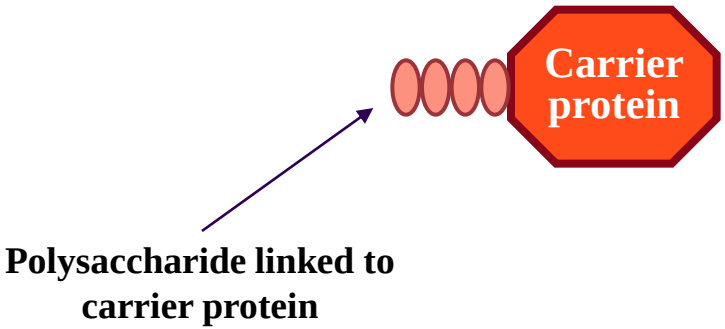
Conjugation

- Some bacteria (e.g. *Haemophilus influenzae type b, Neisseria meningitidis, Streptococcus pneumoniae*) have an outer coating of sugar molecules (called polysaccharides)
- Polysaccharide coatings make it difficult for a baby or young child's immature immune system to see and respond to the bacterium inside
- Polysaccharide vaccines are poorly immunogenic in children under 2 years old and do not stimulate long term immunological memory
- Conjugate vaccines have enabled us to effectively protect children against Hib, Men C and pneumococcal diseases

Conjugation



Conjugate vaccine



Conjugation is the process of attaching (linking) the polysaccharide antigen to a protein carrier (e.g. diphtheria or tetanus) that the infant's immune system already recognises in order to provoke an immune response

Combination Vaccines

- Many vaccines are combined to make it easier to give several vaccines at one time
- Combination vaccines reduce both number of clinic visits and number of injections needed
- Before combination vaccines are licensed, studies are carried out to ensure that:

- the immune response to any of the combined antigens is just as good as the response to the individual vaccines

- the rates of adverse reactions are the same as they would be if the vaccines were administered separately

Vaccine composition

In addition to the antigen, vaccines may contain some or all of the following components:

Component	Purpose	Example
Adjuvants	enhance the immune response to a vaccine	aluminium salts
Preservatives	prevent bacterial or fungal contamination of vaccine	thiomersal
Additives	stabilise vaccines from adverse conditions such as freeze-drying or heat, thereby maintaining a vaccine's potency	gelatine
Residuals from manufacturing process	Inactivating agents Antibiotics - prevent bacterial contamination during manufacturing process Egg proteins- some vaccine viruses are grown in chick embryo cells Yeast proteins	formaldehyde neomycin, streptomycin, polymyxin B influenza, yellow fever HepB vaccine

Stages of Vaccine Trials

Vaccine research and development is a carefully controlled and very lengthy process

Vaccines are rigorously tested to ensure quality, safety and efficacy

The development process starts with extensive laboratory testing

Before trials begin in humans, regulatory bodies must approve laboratory results and give ethical approval

Vaccines then pass through 4 phases of vaccine evaluation in humans

Vaccine trials

Phase I studies

healthy adult volunteers, n = 20-30

Aim: To assess safety and obtain limited immunogenicity data

Phase II studies

subjects in target age group for vaccine e.g. infants n =100-200

Aim: To assess common reactions and obtain immunogenicity data

- assesses dose response
- comparison with current vaccine

Phase III studies

subjects in target population, n depends on incidence/risk of disease

Aim: To assess protective efficacy, identify laboratory correlates of protection, assess rarer reactions

Phase IV surveillance

post-licensure

Studies of new vaccines do not stop at point of licensure

-The number of subjects in Phase I-III is too small to detect rare events

Even once a vaccine is in use, ongoing studies are needed to detect rarer adverse events because in real life administration, compared to pre-licensure trials, there will be:

–variability in preparation

–variability in stability and storage

–and vaccines will be used in different groups than pre-license studies

Vaccine effectiveness

Following licensure, effectiveness of vaccines is monitored through:

- surveillance of disease incidence and
- ascertaining vaccination status of individuals with disease

No vaccine is 100% effective and the effectiveness of each vaccine varies

For this reason, more than one dose and booster doses of vaccine are recommended

e.g. about 90% of people given MMR vaccine will seroconvert after 1 dose of vaccine

A 2nd dose is therefore recommended so that those not protected after the first dose have a second opportunity to make antibodies

Vaccine failures

Primary failure

an individual fails to make an adequate immune response to the initial vaccination (e.g. in about 10% of measles and mumps vaccine recipients)

Secondary failure

an individual makes an adequate immune response initially but then immunity wanes over time (a feature of most inactivated vaccines, hence the need for boosters)

Commonly reported reactions following immunisation

Local Reactions

Pain, swelling or redness at injection site

Small nodules may form at injection site

General Reactions

Fever, irritability, malaise, fatigue, headache, nausea, vomiting, diarrhoea, loss of appetite

Timing of Vaccine Reactions

Inactivated vaccines: generally within 48hrs following vaccination

Live vaccines: occur according to time taken for virus to replicate

e.g. MMR vaccine:

reactions to measles component (malaise, fever, rash) tend to occur 6 to 11 days following vaccination

reactions to rubella component (pain, stiffness or swelling of joints) tend to occur in 2nd week following vaccination

reactions to mumps component (parotid swelling) tend to occur in 3rd week following vaccination (although may occur up to 6 weeks following vaccination)

Adverse events

Live vaccines: frequency of adverse events falls with number of doses

Eg MMR

Because if antibody is made in response to first dose of live vaccine, it neutralises the small amount of vaccine virus in any subsequent vaccine dose

Inactivated vaccines: frequency of adverse events increases with number of doses

Eg tetanus, pertussis

Because if antibody levels are good following previous vaccination, the antibody binds to the vaccine antigen in a subsequent dose of vaccine making an inflammatory response (such as a sore arm).

Minimum slide set created by:

Immunisation Department,

Centre for Infections,

Health Protection Agency

to assist teaching of the *Core Curriculum for Immunisation Training*

(see http://www.hpa.org.uk/infections/topics_az/vaccination/training_menu.htm)