Immunization

Dr Rasha Salama
PhD. Community medicine
Suez Canal University
Egypt
Immunity

Specific defenses

Active immunity
- Following clinical infection
- Following subclinical infection
- Following vaccination

Passive immunity
- Transfer of maternal Antibodies Through placenta
- Transfer of maternal Antibodies Through milk
- Following administration of Immunoglobulin or antiserum

natural
acquired
Active immunity

- Resistance developed in response to stimulus by an antigen (infecting agent or vaccine) and is characterized by the production of antibodies by the host.
Passive immunity

- Immunity conferred by an antibody produced in another host. It may be acquired naturally or artificially (through an antibody-containing preparation).
Immunizing agents

- Vaccines
- Immunoglobulins
- Antisera
Immunoglobulins

• There are 5 major classes: IgM, IgA, IgG, IgE, IgD.

• Two types of immunoglobulin preparations are available for passive immunization:
  – Normal human immunoglobulin
  – Specific (hyper-immune) human immunoglobulin
Antisera or antitoxins

- These are materials prepared in animals or non human sources such as horses.
# Immunoglobulin and antiserum

<table>
<thead>
<tr>
<th>Human normal immunoglobulin</th>
<th>Human specific immunoglobulin</th>
<th>Non human ig (antisera)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis A</td>
<td>Hepatitis B</td>
<td>Diphtheria</td>
</tr>
<tr>
<td>Measles</td>
<td>Varicella</td>
<td>Tetanus</td>
</tr>
<tr>
<td>Rabies</td>
<td></td>
<td>Gas gangrene</td>
</tr>
<tr>
<td>Tetanus</td>
<td>Diphtheria</td>
<td>Botulism</td>
</tr>
<tr>
<td>Mumps</td>
<td></td>
<td>Rabies</td>
</tr>
</tbody>
</table>
Vaccination

• Vaccination is a method of giving antigen to stimulate the immune response through active immunization.

• A vaccine is an immuno-biological substance designed to produce specific protection against a given disease.

• A vaccine is “antigenic” but not “pathogenic”.
Types of vaccines

- Live vaccines
- Attenuated live vaccines
- Inactivated (killed vaccines)
- Toxoids
- Polysaccharide and polypeptide (cellular fraction) vaccines
- Surface antigen (recombinant) vaccines.
Live vaccines

• Live vaccines are made from live infectious agents without any amendment.
• The only live vaccine is “Variola” small pox vaccine, made of live vaccinia cow-pox virus (not variola virus) which is not pathogenic but antigenic, giving cross immunity for variola.
Live attenuated (avirulent) vaccines

• Virulent pathogenic organisms are treated to become attenuated and avirulent but antigenic. They have lost their capacity to induce full-blown disease but retain their immunogenicity.

• Live attenuated vaccines should not be administered to persons with suppressed immune response due to:
  – Leukemia and lymphoma
  – Other malignancies
  – Receiving corticosteroids and anti-metabolic agents
  – Radiation
  – pregnancy
Inactivated (killed) vaccines

- Organisms are killed or inactivated by heat or chemicals but remain antigenic. They are usually safe but less effective than live attenuated vaccines. The only absolute contraindication to their administration is a severe local or general reaction to a previous dose.
Toxoids

• They are prepared by detoxifying the exotoxins of some bacteria rendering them antigenic but not pathogenic. Adjuvant (e.g. alum precipitation) is used to increase the potency of vaccine.

• The antibodies produced in the body as a consequence of toxoid administration neutralize the toxic moiety produced during infection rather than act upon the organism itself. In general toxoids are highly efficacious and safe immunizing agents.
Polysaccharide and polypeptide (cellular fraction) vaccines

- They are prepared from extracted cellular fractions e.g. meningococcal vaccine from the polysaccharide antigen of the cell wall, the pneumococcal vaccine from the polysaccharide contained in the capsule of the organism, and hepatitis B polypeptide vaccine.

- Their efficacy and safety appear to be high.
Surface antigen (recombinant) vaccines.

- It is prepared by cloning HBsAg gene in yeast cells where it is expressed. HBsAg produced is then used for vaccine preparations.

- Their efficacy and safety also appear to be high.
# Types of vaccines

<table>
<thead>
<tr>
<th>Live vaccines</th>
<th>Live Attenuated vaccines</th>
<th>Killed Inactivated vaccines</th>
<th>Toxoids</th>
<th>Cellular fraction vaccines</th>
<th>Recombinant vaccines</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Small pox variola vaccine</td>
<td>• BCG</td>
<td>• Typhoid oral</td>
<td>• Typhoid</td>
<td>• Diphtheria</td>
<td>• Meningococcal polysaccharide vaccine</td>
</tr>
<tr>
<td></td>
<td>• Plague</td>
<td>• Cholera</td>
<td>• Plague</td>
<td>• Tetanus</td>
<td>• Pneumococcal polysaccharide vaccine</td>
</tr>
<tr>
<td></td>
<td>• Oral polio</td>
<td>• Pertussis</td>
<td>• Rabies</td>
<td></td>
<td>• Hepatitis B polysaccharide vaccine</td>
</tr>
<tr>
<td></td>
<td>• Yellow fever</td>
<td>• Salk polio</td>
<td>• Salk polio</td>
<td></td>
<td>• Hepatitis B polypeptide vaccine</td>
</tr>
<tr>
<td></td>
<td>• Measles</td>
<td>• Intra-</td>
<td>• Influenza</td>
<td></td>
<td>• Hepatitis B vaccine</td>
</tr>
<tr>
<td></td>
<td>• Mumps</td>
<td>muscular</td>
<td>• Japanise</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Rubella</td>
<td>influenza</td>
<td>encephalitis</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Intranasal Influenza</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Typhus</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Routes of administration

- Deep subcutaneous or intramuscular route (most vaccines)
- Oral route (sabine vaccine, oral BCG vaccine)
- Intradermal route (BCG vaccine)
- Scarification (small pox vaccine)
- Intranasal route (live attenuated influenza vaccine)
Scheme of immunization

• Primary vaccination
  – One dose vaccines (BCG, variola, measles, mumps, rubella, yellow fever)
  – Multiple dose vaccines (polio, DPT, hepatitis B)

• Booster vaccination
  To maintain immunity level after it declines after some time has elapsed (DT, MMR).
Periods of maintained immunity due to vaccines

- Short period (months): cholera vaccine
- Two years: TAB vaccine
- Three to five years: DPT vaccine
- Five or more years: BCG vaccine
- Ten years: yellow fever vaccine
- Solid immunity: measles, mumps, and rubella vaccines.
Levels of effectiveness

- Absolutely protective (100%): yellow fever vaccine
- Almost absolutely protective (99%): Variola, measles, mumps, rubella vaccines, and diphtheria and tetanus toxoids.
- Highly protective (80-95%): polio, BCG, Hepatitis B, and pertussis vaccines.
- Moderately protective (40-60%) TAB, cholera vaccine, and influenza killed vaccine.
The Cold Chain

• The "cold chain" is a system of storage and transport of vaccines at low temperature from the manufacturer to the actual vaccination site.

• The cold chain system is necessary because vaccine failure may occur due to failure to store and transport under strict temperature controls.
The Cold Chain Equipment

Cold chain equipment consists of the following:

(a) *Walk in cold* rooms: They are located at regional level, meant to store vaccines up to 3 months and serve districts.

(b) *Deep freezers (300 ltr) and Ice lined Refrigerators*: supplied to all districts and the WIC locations to store vaccines. Deep freezers are used for making ice packs and to store OPV and measles vaccines.

(c) *Small deep freezers and ILR (140 ltr)*: One set is provided to PHCs, and Family Planning Centers
• **(d) Cold boxes:** Cold boxes are supplied to all peripheral centers. These are used mainly for transportation of the vaccines.

• **(e) Vaccine carriers:** Vaccine carriers are used to carry small quantities of vaccines (16-20 vials) for the out of reach sessions. 4 fully frozen ice packs are used for lining the sides, and vials of DPT, DT, TT and diluents should not be placed in direct contact with frozen ice packs. The carriers should be closed tightly.

• **(f) Ice packs:** The ice packs contain water and no salt should be added to it.
• Among the vaccines, polio is the most sensitive to heat, requiring storage at minus 20 degree C.
• Vaccines which must be stored in the freezer compartment are: polio and measles.
• Vaccines which must be stored in the COLD PART but never allowed to freeze are: typhoid, DPT, tetanus toxoid, DT, BCG and diluents.
HAZARDS OF IMMUNIZATION

• No immune response is entirely free from the risk of adverse reactions or remote squeal. The adverse reactions that may occur may be grouped under the following heads:

1. Reactions inherent to inoculation
2. Reactions due to faulty techniques
3. Reactions due to hypersensitivity
4. Neurological involvement
5. Provocative reactions
6. Others
• **1. Reactions inherent to inoculation:**
  These may be local general reactions. The local reactions may be pain, swelling, redness, tenderness and development of a small nodule or sterile abscess at the site of injection.

• The general reactions may be fever, malaise, headache and other constitutional symptoms. Most killed bacterial vaccines (e.g., typhoid) cause some local and general reactions. Diphtheria and tetanus toxoids and live polio vaccine cause little reaction.
• **2. Reactions due to faulty techniques:**

Faulty techniques may relate to
• faulty production of vaccine (e.g. inadequate inactivation of the microbe, inadequate detoxication),
• too much vaccine given in one dose,
• improper immunization site or route,
• vaccine reconstituted with incorrect diluents,
• wrong amount of diluent used,
• drug substituted for vaccine or diluent,
• vaccine prepared incorrectly for use (e.g., an adsorbed vaccine not shaken properly before use),
• vaccine or diluent contaminated,
• vaccine stored incorrectly,
• contraindications ignored (e.g. a child who experienced a severe reaction after a previous dose of DPT vaccine is immunized with the same vaccine),
• reconstituted vaccine of one session of immunization used again at the subsequent session.
• Use of improperly sterilized syringes and needles carry the hazard of hepatitis B virus, and staphylococcal and streptococcal infection
3. **Reactions due to hypersensitivity:**

- Administration of antisera (e.g., ATS) may occasionally give rise to anaphylactic shock and serum sickness. Many viral vaccines contain traces of various antibiotics used in their preparation and some individuals may be sensitive to the antibiotic which it contains. Anaphylactic shock is a rare but dangerous complication of injection of antiserum. There is bronchospasm, dyspnoea, pallor, hypotension and collapse.

- The symptoms may appear within a few minutes of injection or may be delayed up to 2 hours. Some viral vaccines prepared from embryonated eggs (e.g., influenza) may bring about generalized anaphylactic reactions. **Serum sickness** is characterized by symptoms such as fever, rash, oedema and joint pains occurring 7 - 12 days of injection of antiserum.
• **4. Neurological involvement:**

• Neuritic manifestations may be seen after the administration of serum or vaccine. The well-known examples are the postvaccinial encephalitis and encephalopathy following administration of anti-rabies and smallpox vaccines.

• Guillain-Barré syndrome in association with the swine influenza vaccine is another example.
5. Provocative reactions:

Occasionally following immunization there may occur a disease totally unconnected with the immunizing agent (e.g., provocative polio after DPT or DT administration against diphtheria).

The mechanism seems to be that the individual is harboring the infectious agent and the administration of the vaccine shortens the incubation period and produces the disease or what may have been otherwise only a latent infection is converted into a clinical attack.
6. *Others:*

These may comprise damage to the fetus (e.g., with rubella vaccination); displacement in the age-distribution of a disease (e.g., a potential problem in mass vaccination against measles, rubella and mumps).
PRECAUTIONS TO BE TAKEN

• Before administration of the antiserum or antitoxin, it is necessary to test for sensitivity reaction. This can be done in 2 ways:
  (a) instilling a drop of the preparation into the conjunctival sac. A sensitized person will develop pricking of the conjunctiva.
  (b) a more reliable way of testing is by intradermal injection of 0.2 ml of antiserum diluted 1 : 10 with saline. A sensitized patient will develop a wheal and flare within 10 minutes at the site of injection. It should be borne in mind that these tests are not infallible.
• Adrenaline (1: 1000 solution) should be kept ready when giving foreign serum. In the event of anaphylaxis, for an adult, 0.5 ml of adrenaline solution should be injected intramuscularly immediately, followed by 0.5 ml every 20 minutes if the systolic blood pressure is below 100 mm of mercury.

• An injection of antihistaminic drug should also be given, e.g., 10-20 mg of chlorpheniramine maleate by the intramuscular route, to minimise the after-effects such as urticaria or oedema. The patient should be observed for 30 minutes after any serum injection.
• The risk of adverse reactions can be reduced by proper sterilization of syringes and needles, by proper selection of the subject and the product, and if due care is exercised in carrying out the procedure. Measles and BCG vaccines should be reconstituted only with the diluent supplied by the manufacturer.

• Reconstituted vaccine should be discarded at the end of each immunization session and NEVER retained for use in subsequent sessions. In the refrigerator of the immunization centre, no other drug and substances should be stored beside vaccines.

• Training of immunization worker and their close supervision to ensure that proper procedures are being followed are essential to prevent complications and deaths following immunization.
Vaccination Coverage

• Vaccination coverage is the percent of at risk or susceptible individuals, or population who have been fully immunized against particular diseases by vaccines or toxoids. To be significantly effective in prevention of disease on mass or community level at least a satisfactory proportion (75% or more) of the at risk population must be immunized.
Ways of achieving satisfactory immunization coverage

• Efficient immunization service; urban and rural

• Health awareness and cooperation of the public

• Periodic mass immunization campaigns, to cover those who missed regular immunizations

• Outreach programs in rural and nomad areas, and home visits
Application of active immunization

- Infants and children expanded immunization program (schedule)
- Active immunization for adult females
- Vaccination for special occupations
- Vaccination for special life styles
- Vaccination for special environmental situations
- Vaccinations for special health status persons
- Vaccinations in travel
- Vaccines against bioterrorism
Compulsory (obligatory) vaccination for infants, and booster vaccination for children (Expanded immunization program)

- See local schedule of vaccination

- Note (children failing to complete childhood vaccination schedule)
Active immunization for adult females

• MMR vaccine is given in adolescence before or after marriage, but not during pregnancy and has to be before 3 months of conception

• Tetanus toxoid in pregnancy to prevent tetanus neonatorum in the newborn. In the first pregnancy on the third month and after 1 month. The third dose in the second pregnancy, and the fourth on the third pregnancy with a maximum of 5 doses. If 10 years elapse, and then pregnancy occurs, the doses are given from the start.

• Live attenuated vaccines should not be given during pregnancy.
Vaccination for special occupations

- Health care workers: hepatitis B, influenza, MMR, polio
- Public safety personnel (police, fire fighters) and staff of institutions for the developmentally disabled: hepatitis B, influenza
- Vets and animal handlers: rabies, plague and anthrax
- Sewage workers: DT, hepatitis A, polio, TAB
- Food handlers: TAB
- Military troops and camp dwellers: pneumococcal, meningococcal, influenza, BCG (for non reactors), tetanus
Vaccination for special life styles and special environmental situations

- Homosexually active males, Heterosexual with promiscus sexual partner specially who has STDs, and Injecting drug users
- Inmates of long term correctional institutes, residents of institutions for the developmentally disabled, and household contacts of HBV carriers or patients

All should receive hepatitis B vaccine
Vaccinations for special health status persons

- Immuno-compromised persons (Leukemia, lymphoma, HIV, malignancy…)
- Hemodialysis and transplantation

Should receive the following vaccines according to their situation:

→ HBV, Influenza, Pneumococcal vaccines
Vaccinations in travel

• Varies according to the country of arrival and departure.
  – Primary vaccine series
  – Continuation of booster doses
  – Specific vaccine according to the country traveled to:
    • TAB, YF, cholera, meningiococcal, pneumococcal, HIB, influenza, rabies, plague, Japanese encephalitis.
    • Haj for instance necessitates meningococcal vaccination from all over, and YF from places like south Africa, and cholera from places like India.
Vaccines against bioterrorism

- Anthrax
- Small pox
- plague
New approaches

• Schistosomiasis
• Cancer
• HIV/AIDS
• Malaria
Vaccine surveillance and testing

“monitoring vaccine effectiveness”

Through:

• Randomized field trials
• Retrospective cohort studies
• Case-control studies
• Incidence density measures
Randomized field trials

– The standard way to measure the effectiveness of a new vaccine introduced.
– In this type of trial, susceptible persons are randomized into two groups and are then given the vaccine or the placebo.
– The vaccinated and the unvaccinated are followed through the high risk season of the year.
Randomized field trials (cont.)

The attack rate (AR) is then determined in each group:

\[ AR = \frac{\text{Number of persons ill}}{\text{Number of persons exposed to the disease}} \]

next the vaccine effectiveness (VE) is calculated:

\[ VE = \frac{\text{AR (unvaccinated)} - \text{AR (vaccinated)}}{\text{AR (unvaccinated)}} \times 100 \]
Retrospective cohort studies

• The antigenic variability of influenza virus necessitates frequent (often yearly) changes in the constituents of the vaccine to keep them up date with the new strains. Retrospective cohort studies are thus done to evaluate the protective efficacy of the vaccines.
Case-control studies

- Done because randomized control trials are very costly.

\[ \text{VE} = 1 - \frac{\text{AR (vaccinated)}}{\text{AR (unvaccinated)}} = (1 - \text{RR}) \text{ or } (1 - \text{OR}) \]
Incidence density measures

- They are used to determine the optimal timing for administration of a new vaccine and the duration of the immunity produced. It has the following formula:

\[ ID = \frac{\text{Number of new cases of a disease}}{\text{Person-time of exposure (days, weeks, months, years..)}} \]
THANK YOU