IMMUNOLOGY

By

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Objectives

At the end of all the sessions on immunology, the students should be able to:

- Define immunology, Immunity and immune system.
- Discuss the importance of immunity and its role in maintenance of normal health and prevention of diseases.
- Describe concepts about immunology in all contexts.
- Apply the knowledge of immunology for Natural and Artificial immunity in medical practice.
Immunology

It is the study of the immune system.

Deals with

- complex defence mechanism of body
- complex invading agent
Immune System

It is system of complex defense mechanisms of the body against complex invading agents.

Multiple host defense mechanisms are stimulated by invading agent.

Overlapping of host defenses determine his susceptibility to infections.
Immunity

It is the state of resistance or insusceptibility of the body to toxic molecules, micro-organisms and foreign cells.
Types of Immunity

- Innate Immunity
  (Natural Immunity or Non-Acquired Immunity)

- Acquired Immunity
Types of Immunity

• Non-Specific Immunity

• Specific Immunity
Innate Immunity (Defence)

It is that immunity or body defence which operates regardless of the individual’s past experience.
Types of Innate Defenses

- Outer Defenses
- Inner Defenses
Types of Innate Defenses (Contd.)

Outer Defenses

- **Mechanical Barriers**
  - Skin
  - Mucous Membrane

- **Mechanical Removal**
  - Coughing
  - Sneezing
  - Sniffing
  - Blinking, sweating etc.
Types of Innate Defenses (Contd.)

- Germicidal secretions
  - Sweat
  - Gastric juice
  - prostatic secretions
  - breast milk etc.

- Normal Flora
Types of Innate Defenses (Contd.)

**Inner Defenses**

- **Body fluids containing**
  - Lysozymes, complements, properidin, B-Lysins etc.
  - Natural antibodies

- **Phagocytes**
  - Lymphocytes, Natural killer cells etc.
Factors influencing Innate Immunity

- Genetic Factors
- Age
- Hormones
- Fatigue/stress
- Temperature
- Nutrition (Undernutrition, malnutrition)
- Injuries, surgical operations, malignancies
- Debilitating conditions like Diabetese, Pregnancy, chronic condition
Acquired (Adaptive) Immunity

It occurs after the exposure of the body to an antigen. It is specific and is mediated either by antibodies or by lymphoid cells.
Characteristics of Acquired Immunity (Defense)

- It takes time to develop
- More powerful
- Varying degrees of immunity
- Specific
- Depends on immunological memory
- Recognition of non-self (foreign)
Types of Acquired Immunity

- Active Immunity
- Passive Immunity
Responses of Acquired Immunity

- Antibody-mediated *(Humoral)* Immunity
- Cell-mediated *(Cellular)* Immunity
Role of Lymphocytes in antibody-mediated (Humoral) Immunity

Bone Marrow Stem Cells

B lymphocytes  Macrophages

Antigen

Plasma Cells

Antibody-mediated immunity
Cellular Immunity

- Mediated by T-Cells
- T-Cells initiate a chain of responses i.e
  - Activation of macrophages
  - Release of cytotoxic factors
  - Mononuclear inflammatory reactions
  - Delayed hypersensitivity reactions
  - Secretion of immunological mediators
Role of Lymphocytes in Cellular Immunity

Bone marrow stem cells

→ Macrophages

→ T-Lymphocytes

→ Antigens

→ Lymphoblasts

→ Cell-mediated immunity
Active Immunity

It is the resistance induced after effective contact with/invasion of foreign antigen, like microorganisms, their products or transplanted cells. The contact may be due to

- Clinical infection
- Sub-clinical infection
- Immunization
- Exposure to microbial products e.g. toxoids
Active Immunity - Advantages

- It is specific for a particular agent.
- It depends upon humoral and cellular responses of the host.
- It provides long-term immunity.
- Less expansive (Vaccines are cheaper than antisera)
Active Immunity - Advantages

- The host’s immune system develops antibodies itself.
- Severe reactions are rare.
- The protective efficacy of active immunization exceeds that of passive immunization.
Active Immunity - Disadvantages

- It has slow onset.
- It needs a prolonged and repeated contact with the antigen.
- It is not helpful for immediate resistance/protection.
- As it is specific, it will not provide protection against more than one antigen.
Types of Active Immunity

- Naturally Acquired Active Immunity
- Artificially Acquired active Immunity
Types of Active Immunity

- **Humoral Immunity** - antibody mediated
- **Cellular Immunity** - Cell-mediated
END OF FIRST LECTURE FOR EVEN BATCH
Passive Immunity

It is produced by the introduction of pre-formed antibodies in the form of antisera or immunoglobulins, obtained from another host.
Passive Immunity
(Advantages)

- Immunity is promptly established
- Useful for those whose immune system is weak or non-functioning
- Helpful in emergencies
- Applicable in post-exposure prophylaxis
Passive Immunity - Disadvantages

- Immunity produced is temporary and short-lived
- No education of reticulo-endothelial system for creation of memory cells
- Immunoglobulins esp. Non-human (Antisera) may cause severe hypersensitivity reaction
Types of Passive Immunity

- Naturally Acquired Passive Immunity
- Artificially acquried Passive Immunity
Means of naturally Acquired passive Immunity

- Tranplacental transfer of antibodies
- Breast Feeding
Types of Artificially acquired Passive Immunity

- Human Immune-globulins
- Non-Human Immune-globulins (anti-sera)
Antigen

Any substance which when introduced into any human or animal tissues, is capable of provoking an immune response.
Antibody

An antibody is an immune-globulin which is produced as a result of introduction of an antigen into the tissues of an animal and can react specifically with that antigen in some demonstrable way.
Immune Person

- A person who posses "specific protective antibodies or cellular immunity as a result of previous infection or immunization."
Immune Response

Primary Response:

- Production of the antibodies (immune-globulins) in response to administration of an antigen for the first time in an un-exposed animal or human.
- First immune-globulin to appear - IgM
- Latent period - 3-10 days
- Duration - rises during 2-3 days and then decline rapidly.
Primary response (contd)

- In case of sufficient stimulus
- IgG antibody appear in few days
- Peak reaches in 7—10 days
- Gradually falls over a period of weeks or months.
Immune Response

Primary Response

Weeks
Primary Response Depends on

- Dose of the antigen
  
  (50 times more dose is required to induce IgG antibodies than that which is required to induce IgM antibody)

- Nature of the antigen

- Route of administration

- Adjuvants

- Nutritional status of the host
Immunological memory

- An important outcome of primary antigenic challenge
- Education of reticuloendothelial system
- Memory cells are produced by both B and T lymphocytes
- Accelerated secondary response is attributed to Immunological memory.
- (the basis of vaccination and revaccination)
Secondary Response (Booster Response)

It is the response to repeated doses of the antigen. There is:

- Short latent period
- Antibody production is rapid
- Antibodies are more abundant
- Antibody level is high and for longer period
- Antibody has more capacity to bind with the antigen.
Immune Response

Primary Response
Secondary Response

Antigen

Weeks
Immune-globulins

Immunoglobulins are that portion of serum which show antibody activity. They are gamma globulins. There are five major types of immunoglobulins.

1. IgG
2. IgM
3. IgA
4. IgD
5. IgE
Immunoglobulins

- **IgG**: 85% of total serum immunoglobulin, can diffuse into interstitial space so mostly extravascular and are transported across placenta.

- **IgM**: 10% of total serum immunoglobulin, promptly formed, indicative of recent infection, high agglutinating and complement fixing ability, half life is 10 days
- **IgA**: 15% of total serum immunoglobulin
  Found in body secretions, provide protection at mucous membrane against local infection, half life is 6–8 days

- **IgD**: half life is 2.8 days, main function is not determined

- **IgE**: half life is 2.3 days, major antibody responsible for immediate allergic anaphylactic reaction
Factors influencing antibody formation

- Number and spacing of doses of antigen.
- Physical state of antigen.
- Route of administration of antigen.
- Dose of antigen.
- Mixture of antigens.
- Age of animal.
- Individual variations.
- Presence of preformed antibodies.
Artificially Acquired active Immunity

Accelerated secondary response is attributed to Immunological memory which makes the basis of vaccination and revaccination.
Vaccine

It is an immuno-biological substance designed to produce specific protection against a disease.

It stimulates production of antibody and other immune mechanisms.
Vaccine

Vaccine may be prepared from

- Live modified organisms
- Inactivated or killed organisms
- Extracted cellular fractions
- Toxoids
- Combination of these

(Recently sub-unit vaccine and recombinant/genetically engineered vaccines are prepared)
Live vaccines

- Prepared from live (generally attenuated) organisms.
- They have lost their ability to produce disease but retain their immunogenicity.
- They are more potent immunizing agents than killed vaccines.
- Examples: BCG, Measles, OPV
Live vaccines (Important notes)

- Proper storage at certain temp is must for live vaccines.
- Live vaccines should not be administered to persons with immune deficiency diseases
- Steroid therapy
- Immunosuppressed conditions
Differences between Live and In-activated Vaccines

- Live Vaccines
  - Vaccine dose is low
  - Long-lasting immunity
  - Immunity level is high
  - Boosters needed infrequently

- In-activated Vaccines
  - Dose is high
  - Short-lived immunity
  - Low
  - Frequently needed
Toxoids

Some micro-organisms produce exotoxins. The toxins produced by these organisms are detoxicated and used in the preparation of the vaccines. The antibodies produced, neutralise the toxic moiety instead of acting upon whole organism.
Common Immunising Agents (Live Attenuated Vaccines)

- **Bacterial**
  - BCG
  - Oral Typhoid
  - Plague

- **Viral**
  - Oral Polio (Sabin)
  - Yellow fever
  - Measles
  - Mumps
  - Rubella
  - Influenza
Common Immunising Agents
(Inactivated/Killed Vaccines)

- **Bacterial**
  - Typhoid
  - Cholera
  - Pertussis
  - Meningitis
  - Plague

- **Viral**
  - Rabies
  - Polio(Salk)
  - Influenza
  - Hepatitis-B
Common Immunising Agents (Toxoids)

- Bacterial
  - Diphtheria
  - Tetanus
Common Immunising Agents (Immunoglobulins)

- Human Normal Immunoglobulins
  - Hepatitis A
  - Measles
  - Rabies
  - Tetanus
  - Mumps
Common Immunising Agents
(Immunoglobulins)

- Human Specific Immunoglobulins
  - Hepatitis B
  - Varicella
  - Diphtheria
Common Immunising Agents
(Immunoglobulins)

- Non-Human Immunoglobulins (Antisera)
  - Diphtheria
  - Tetanus
  - Gas Gangrene
  - Botulism
  - Rabies
Cold Chain

It is the system of storage and transport of vaccines at low temperature from the manufacturer to the actual site of vaccination.
Cold Chain

- Components of Cold Chain:
  - Walk in cold rooms
  - Deep Freezers & ILR
  - Small Deep Freezers & ILR
  - Cold Box
  - Vaccine Carrier
  - Flasks/Day Carriers
  - Ice-Packs
Hazards of vaccination

- Reactions due to inoculation
  - Local
  - General
- Reactions due to faulty technique
- Reactions due to hypersensitivity
- Neurological problems
- Provocative Reactions
- Others
PRECAUTIONS & CONTRA-INDICATION FOR IMMUNISATION
Herd Immunity

It is the level of immunity or resistance of the community or a group of people to a particular disease. It is immunity of the community as a whole. It provides immunological barrier against disease in human herd.
Herd Immunity

- Contributing Factors:
  - Clinical or Sub-Clinical Infection
  - Immunisation
  - Herd Structure
Expanded Programme on Immunisation

- Essentials of a Public Health Programme at Mass Level
  - Epidemiologically relevant
  - Immunologically effective
  - Operationally feasible
  - Socially acceptable
Expanded Programme on Immunisation

It is a global programme targeted at reduction of morbidity and mortality from six childhood diseases which are preventable by immunisation.

1974: WHA passed resolution and directed WHO to carry out the activities of this programme.
Expanded Programme on Immunisation

1978: Pakistan started as a pilot project in Rawalpindi/Islamabad.

1979: Started in whole of the country
Expanded Programme on Immunisation

- Target Diseases
  - Tuberculosis
  - Poliomyelitis
  - Diphtheria
  - Tetanus
  - Pertussis
  - Measles &
  - Hepatitis-B
Expanded Programme on Immunisation (EPI)

- Objectives:

The overall objectives of the EPI is reduction of morbidity and mortality from the six target diseases by offering immunisation services.
Expanded Programme on Immunisation (EPI)

The specific objectives are:

- Attaining 100% immunisation coverage.
- Elimination of Neonatal Tetanus.
- 95% reduction of Measles incidence.
- Eradication of poliomyelitis.
- Reduction in the incidence of Diphtheria, Pertussis and Tuberculosis,
- Controlling other diseases by the introduction of newer vaccines in the programme like Hepatitis-B vaccine.
## Immunisation Schedule-EPI

<table>
<thead>
<tr>
<th>Age</th>
<th>Vaccine</th>
<th>Dose</th>
<th>Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>At Birth</td>
<td>BCG</td>
<td>0.05/0.1 ml</td>
<td>intradermal</td>
</tr>
<tr>
<td>At Birth</td>
<td>OPV-Zero</td>
<td>2 drops</td>
<td>oral</td>
</tr>
<tr>
<td>At 6 weeks</td>
<td>DPT-1</td>
<td>0.5 ml</td>
<td>intramuscular</td>
</tr>
<tr>
<td>At 6 weeks</td>
<td>OPV-1</td>
<td>2 drops</td>
<td>Oral</td>
</tr>
<tr>
<td>At 6 weeks</td>
<td>HBV-1</td>
<td>0.5 ml</td>
<td>intramuscular</td>
</tr>
<tr>
<td>Age</td>
<td>Vaccine</td>
<td>Dose</td>
<td>Route of administration</td>
</tr>
<tr>
<td>-------------------</td>
<td>---------</td>
<td>---------</td>
<td>-------------------------</td>
</tr>
<tr>
<td>At 10 weeks</td>
<td>DPT-2</td>
<td>0.5 ml</td>
<td>intramuscular</td>
</tr>
<tr>
<td>At 10 weeks</td>
<td>OPV-2</td>
<td>2 drops</td>
<td>Oral</td>
</tr>
<tr>
<td>At 10 week</td>
<td>HBV-2</td>
<td>0.5 ml</td>
<td>intramuscular</td>
</tr>
<tr>
<td>At 14 weeks</td>
<td>DPT-3</td>
<td>0.5 ml</td>
<td>intramuscular</td>
</tr>
<tr>
<td>At 14 weeks</td>
<td>OPV-3</td>
<td>2 drops</td>
<td>Oral</td>
</tr>
<tr>
<td>At 14 weeks</td>
<td>HBV-3</td>
<td>0.5 ml</td>
<td>intramuscular</td>
</tr>
<tr>
<td>At 9 &amp; 15 months</td>
<td>Measles</td>
<td>0.5 ml</td>
<td>Sub-cutaneous</td>
</tr>
</tbody>
</table>
Tetanus immunisation of women of child-bearing age

<table>
<thead>
<tr>
<th>No. of dose</th>
<th>Dose</th>
<th>Route of administration</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>TT1</td>
<td>0.5 ml</td>
<td>Intramuscular</td>
<td>At first contact</td>
</tr>
<tr>
<td>TT2</td>
<td>0.5 ml</td>
<td>Intramuscular</td>
<td>4 weeks after TT1</td>
</tr>
<tr>
<td>TT3</td>
<td>0.5 ml</td>
<td>Intramuscular</td>
<td>6 months after TT2</td>
</tr>
<tr>
<td>TT4</td>
<td>0.5 ml</td>
<td>Intramuscular</td>
<td>1 year after TT4</td>
</tr>
<tr>
<td>TT4</td>
<td>0.5 ml</td>
<td>Intramuscular</td>
<td>1 year after TT4</td>
</tr>
</tbody>
</table>
Individual Vaccines

**BCG Vaccine**
- Live attenuated vaccine
- Freeze-dried vaccine
- Vaccine stored at sub-zero temperature
- Diluent solution stored at 4-8 degree C
- Prepared immediately before administration
- Discarded if not used within half an hour after preparation
BCG Vaccine

- Given intradermally in dose 0.05ml to newborns and 0.1ml after one month of age.
- Specifically effective for childhood tuberculosis, Milliary Tuberculosis and tuberculous meningitis
- In low incidence countries vaccine given to Mantoux negative people
- Provides protection for 7-10 years.
BCG Vaccine

- Complications:
  - Supporative Lymphadenitis
  - Disseminated infection
  - BCG Osteitis
  - Abscess formation at the site of injection
BCG Vaccine

- Contra-indications:
  - Patients suffering from Eczema, infective dermatitis.
  - Hypogammaglobulinaemia.
  - Persons with history of Immunodeficiency.
Polio Vaccines

- **Oral Polio Vaccine (OPV)**
  - Sabin vaccine

- **Inactivated Polio Vaccine (IPV)**
  - Salk Vaccine
OPV

- Live attenuated vaccine
- Contains three main types of polio viruses
- Given orally.
- Vaccine stimulates antibody production locally in gut (IgA) as well as systemically in blood (IgG & IgM)
- Protects against Gastrointestinal as well as paralytic polio.
OPV

- Contra-indications
  - Acute diarrhoeal states
  - Three months after tonsillectomy
  - Hot fluids and hot milk should not be ingested for half an hour after vaccination.
  - There is no restriction of Breast Feeding after vaccination
Measles-Mumps-Rubella (MMR)

- Triple vaccine
- Freeze died vaccine
- Measles vaccine is given at 9 months age if given alone
- MMR is given at the age of one year or more
- Dose – 0.5 ml given subcutaneously
Anti-Rabies Vaccines

- All Anti-Rabies vaccines are inactivated
- Nervous Tissue Vaccines
  - Sheep brain vaccine (Semple vaccine)
  - Suckling mouse Brain Vaccine
- Avian Embryo Vaccine
  - Duck embryo vaccine
  - Chick embryo vaccine
- Cell Culture Vaccine
  - Human Diploid Vaccine (HDCV)
  - Second Generation Tissue Culture Vaccine (DCV)
Diploid Cell Vaccine (DCV)

- Highly effective, safe but costly vaccine.
- Freeze dried vaccine.
- Dose: 1.0ml - intramuscular in 3-5 doses
- Given in pre and post-exposure prophylaxis
- Rabies immunoglobulin sand/or Rabies anti-serum is also recommended along with vaccine in case of post-exposure prophylaxis.
Diploid Cell Vaccine (DCV)

- Contra-indications
  - Erythema, itching, swelling at the site of injection in about 25% of vaccinees.
  - Headache, nausea, malaise and myalgia in rare cases.
  - No serious complication.

- Street Virus-Fixed virus
Yellow Fever Vaccine

- Live attenuated vaccine
- Freeze-dried vaccine
- Store at sub-zero temperature
- Reconstituted with diluent solution at the time of use
- Discarded if not used within half an hour
- Dose-0.5ml given subcutaneously-single dose
Yellow Fever Vaccine

- Immunity develops in 10 days and persists for 10 years
- Recommended for those going to endemic areas, tropical countries like Africa & South America or coming to non-endemic countries like Pakistan
- Not recommended for children because of higher risk of developing encephalitis
Yellow Fever Vaccine

- Complications:
  - Fever
  - Body aches
  - Encephalitis
Hepatitis-B Vaccine

- Types:
  - Plasma-derived vaccine
  - Recombinant DNA-Yeast derived vaccine
  - Dose: Adults: 20 microgram (1ml)
    - Children: 10 microgram (0.5ml)
    - Given intramuscularly
Hepatitis-B Vaccine

- Vaccine given in three doses at 0, 1 and 6 month. Booster given after 5 years.
- In case of emergency given at 0, 1 and 2 month. Booster given after one year.
- Provides about 95% protection to the vaccinees.
- Vaccine given to high risk groups like pathologists, heamatologists, laboratory workers, blood bank workers surgeons etc.
Typhoid Fever Vaccines

- **Killed/Inactivated Vaccines**
  - TAB (Trivalent) Vaccine
  - Bivalent Vaccine
  - Monovalent Vaccine
  - Typhim Vi Vaccine

- **Live attenuated Vaccine**
  - Viviotif (oral capsules)
Cholera Vaccine

- Killed/Inactivated vaccine

- Efficacy only 50%

- Not recommended for epidemics

- Dose: 2ml given intramuscularly in two doses at interval 4 weeks
Influenza Vaccines

- **Killed Vaccine**
  - Single dose.
  - Dose; 0.5 ml given subcutaneously

- **Live attenuated vaccine**
  - Given as nasal drops

- **Split-virus vaccine**

- **Neuraminidase-specific vaccine**

- **Recombinant vaccine**
Meningococcal Vaccine

- Effective against *Neisseria Meningitidis*
- Inactivated vaccine
- Monovalent (A or C) vaccine
- Polyvalent (A-C: A-C-Y etc.)
- Immunity lasts for three years
Other Vaccines

- Plague
- Haemophilus influenzae-B
- Rota virus
Anti-Rabies Vaccine
RABIES VACCINE (Killed Virus)
5% Sheep Brain Suspension in 0.5% Carbol Saline

Government Supply Not for Sale

National Institute of Health
Islamabad Pakistan
Measles Vaccines
Polio vaccines
Hepatitis-B Vaccine
DPT Vaccines
BCG Vaccine
Anti-tetanus Serum (ATS)
Anti-Snake Serum
Nimra, student of class VI, while returning from school is bitten by a stray dog on her face and hands. The dog ran away after biting. As a casualty medical officer,

1. What possible disease/s do you expect
2. What immunising agents will you advise
3. What will be schedule for active immunity
Nimra, student of class VI, while returning from school is bitten by a stray dog on her face and hands. The dog ran away after biting. As a casualty medical officer

- What possible disease(s) do you expect
- What immunising agents will you advise
- What will be schedule for active immunity
Dr. Nauman is going to Nairobi to attend a three week training on Haemorrhagic fevers. He is already vaccinated for HBV.

- What vaccine do you recommend for him and when?
- What is the dosage schedule of that vaccine?
- What restrictions will he have to face during this trip if he does not have any vaccination proof.
Live & inactivated vaccines are available against

- Measles
- Tuberculosis
- Yellow fever
- Poliomyelitis
- Cholera
Human Specific Ig as well as Non-Human Ig (Anti-sera) is available against

- Tetanus
- Diphtheria
- Hepatitis-B
- Measles
- Varicella